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AEROMEDICAL REVIEW

RESPIRATOR QUALITATIVE/QUANTITATIVE FIT TEST METHOD ANALYSIS

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This technical report has been reviewed and is approved for publication.

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This report analyzes the qualitative and quantitative methods to measure the fit of a respirator to a user. In particular, both gaseous and aerosol (liquid and solid) quantitative challenge agents are studied. The human compatibility of qualitative and quantitative challenge agents is developed. A final recommendation for a qualitative and quantitative respirator fit test method and procedure is made.

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PREFACE

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CONTENTS

RESPIRATOR QUALITATIVE/QUANTITATIVE FIT TEST METHOD ANALYSIS

INTRODUCTION

The importance of training users to obtain the best possible fit of a respirator to their face is a serious concern in governmental and civilian/industrial sectors. It is vital that users understand the capability of a respirator they are required to wear and the degree of protection they can expect from it. Most importantly, users must be confident that respirators can be fitted in a reproducible manner. Several methods exist for testing the fit of a respirator. The final determination of respirator facepiece fit should include a combination of qualitative and quantitative fit tests. Qualitative fit testing relies on the user's subjective response to a physical/chemical challenge of the facepiece fit. A quantitative fit test employs sensitive detection instrumentation to actually measure the face-to-facepiece leakage of a chemical challenge agent. The methods and analyses presented in this report apply to negative-pressure, nonpowered, quarter-, half-, and full-face respirator devices.

QUALITATIVE FIT TEST METHODS

Negative Pressure Test

This test requires no special equipment and can be used with any respirator whose filter canister inlet can be covered. To implement this test, the user dons the respirator and occludes the inlet opening of the canister by covering it with the palm of the hand or by replacing the canister's tape seal. The user then inhales and holds the breath for 10 sec so that the facepiece collapses slightly. If the facepiece remains collapsed, and no inward leakage of air is detected, the face-to-facepiece seal is considered satisfactory (214, 284, 286, 295).

Positive Pressure Test

This test is normally accomplished immediately after the negative pressure test. To implement this test, the user dons the respirator, the exhalation valve is closed, and the user exhales gently into the facepiece. The fit is considered satisfactory if a slight positive pressure can be sustained inside the facepiece without any evidence of outward leakage of air at the face-to-facepiece seal (214, 284, 286, 295).

Isoamyl Acetate (Banana Oil) Test

Isoamyl acetate has a pleasant, easily-detectable odor that makes it an excellent chemical challenge agent for qualitatively checking respirator fit.

There are at least two versions of the isoamyl acetate qualitative fit test. The simplest version of this test involves saturating a piece of cotton or cloth with the liquid and passing it close to the respirator face-to-facepiece sealing surface, taking care not to touch the user's skin. A more complex version of this test involves the use of a room, small booth, or hood that covers the user's head and shoulders. A known concentration of isoamyl acetate vapor, approximately 100 parts-per-million (ppm), is generated by evaporating 17.3 ml of the liquid for each 1000 ft^3 (about 28 m^3) of enclosed volume. Since most people have an isoamyl acetate odor threshold of 1-10 ppm, and the exposure limit is 100 ppm, a fixed challenge concentration helps to reduce the number of variables involved with this test. For either version of this test, it is important to ensure the respirator is equipped with an organic vapor cartridge/canister (117, 214, 284, 286).

Stannic Chloride/Titanium Tetrachloride Test

This test exposes the user to an irritating aerosol produced by a commercially available smoke tube. These tubes are approximately 12 cm long by 1 cm in diameter and are filled with either stannic chloride or titanium tetrachloride impregnated pumice. To implement this test, the user dons a respirator and closes his eyes while an assistant breaks open the ends of a smoke tube and passes air through it. An irritating smoke is produced consisting of hydrochloric acid absorbed on small solid particles. The smoke is directed at the facepiece seal, and leakage is detected by the user's involuntary coughing or sneezing caused by irritation of the throat and lungs. This test should only be performed when proper safeguards are taken, such as providing exhaust ventilation in the area of the test and protecting the assistant administering the test (214, 284, 286).

Miscellaneous Research and Development Qualitative Tests

Other qualitative fit tests have been investigated, but have not received as extensive use as those mentioned above. In one, a stream of talcum powder or coal dust is directed around the face-to-facepiece seal. The user then removes the respirator and leakage is revealed by telltale streaks of the powder or dust. Another test involves spraying uranine (a fluorescein dye) around the respirator sealing surface. The respirator is then removed and leakage is detected using a fluorescent light source. Finally, the U.S. Army has experimented with a method that uses a 1450 mg/m^3 concentration of chloropicrin (trichloronitromethane [PS]) as an odor-sensitive, vapor-challenge agent. A leak is considered to have occurred if the user can detect the odor of PS (15, 214, 284).

QUANTITATIVE FIT TEST METHODS

All current respirator quantitative fit test (QNFT) performance evaluations involve placing the respirator user in an atmosphere containing an easily detectable, relatively nontoxic gas, vapor, or aerosol. The atmosphere inside the respirator is sampled through a probe carefully fitted to sample the atmosphere in the oral/nasal or visual cavity. Leakage is expressed as a

ratio of the ambient challenge atmosphere concentration outside the respirator to that sampled from the interior of the respirator. This ratio is called the protection factor (PF) (99, 214).

Since the beginning of respirator quantitative fit testing, users and manufacturers have expressed concern that leakage of an aerosol might be significantly different from that of a vapor challenge agent and that the PFs calculated using an aerosol challenge agent might not predict the level of protection for gaseous contaminants. This concern has been studied by two independent laboratories (49, 52, 72, 97, 104). One United Kingdom study compared the leakage of a submicron aerosol of sodium chloride to the gas Arcton-12 (Freon-12 or dichlorodifluoromethane) and found that the leakages for full- and half-face respirators were comparable (97). In another United Kingdom study, the leakage of a submicron aerosol of sodium chloride was compared to argon, and the results for a demand self-contained breathing apparatus (SCBA) respirator were similar (52, 72, 104). Finally, a study by the Los Alamos Scientific Laboratory (LASL) compared the leakage of sulfur hexafluoride to a submicron aerosol of sodium chloride and di-2-ethylhexyl phthalate (DEHP) (commonly, but erroneously referred to as dioctyl phthalate) and found that the results for two types of half-face respirators were similar (149).

Quantitative Gaseous Challenge Agent Fit Test Methods

Argon--The British Safety in Mines Research Establishment has devised a dynamic method to measure the leakage of full-face respirators while the subject performs various exercises. In this test, the user dons a respirator (complete with two breathing tubes) and is placed inside a transparent plastic hood which is sealed around the waist. Pure argon is delivered into the top of the hood from a regulated cylinder supply to maintain hood pressure slightly above atmospheric. Argon is used as the challenge agent because it is physiologically inert, inexpensive, and commercially available in a pure form. To implement this test, the user inhales oxygen (medical quality) supplied from a cylinder fitted with a pressure reducer and demand valve. The oxygen breathing tube is fitted with a sampling port and a valve to control the direction of flow; a spirometer measures the volume of oxygen used. The exhaled gas flows through the other breathing tube into a sampling bladder that is fitted with a sampling port; excess exhaled gas is allowed to vent to the atmosphere. The amount of argon in the exhaled gas (corrected for basal retention of 0.93%) is measured with a mass spectrometer. This instrument is capable of measuring the differential amount of argon present in the exhaled breath to a concentration of 10 ppm. A multiway tap is connected to the mass spectrometer and the various sampling ports. Sampling is accomplished using a small suction pump. This method has been implemented to measure respirator leakages on the order of 0.001% (36, 52, 72).

Ethylene--National Draeger Incorporated has developed two versions of the Model 80 facemask fit-test device. One uses a detector tube and the other uses an electronic leak detector instrument. To implement a quantitative respirator fit test, the user dons a mask and slips a transparent plastic hood over the head and seals it around the neck. An air mixture containing ethylene (2% by volume) is used as a challenge gas. The mixture is allowed to flow into the hood from a regulated cylinder supply. An exhaust port is used to

thoroughly flush the hood with the inflowing ethylene gas mixture; this procedure ensures the composition of the challenge gas in the hood is a 2% by volume concentration of ethylene. To detect the challenge gas in the user's exhaled breath, a specially configured sample cell is attached to the exhalation valve. This cell has a low flow resistance valve which opens only during the actual exhalation phase. Measuring the challenge gas concentration in the plastic hood is normally dispensed with because after the purging procedure, the concentration in the hood is assumed to differ insignificantly from the supply challenge gas mixture. Proof of a tight face-to-facepiece seal is established by measuring the concentration of the challenge gas in the exhaled breath. A detector tube is used for this measurement; it has a detection range from 0.5 to 10 ppm of ethylene. Thus, respirator fit leakage in the range 0.0025% to 0.05% can be detected based on a 2% volume challenge gas concentration. In place of the ethylene detector tube, an electronic leak detector instrument is available for simultaneously measuring the concentration of challenge gas in the hood and exhaled breath. However, when using the electronic leak detector scheme, a 2% mixture of sulfur hexafluoride in air is used as the challenge gas instead of the ethylene mixture. The electronic leak detector is an electron capture device. The beta radiation source of the detector generates (ionization) free electrons in the sampled exhaled gas. These electrons produce a current between two electrodes. A change in the measured current is directly related to the concentration of the challenge gas. Sampling the exhalation and hood gas are performed simultaneously. Detector sensitivity is approximately the same as the detector tube version. The presence of the radiation source in this detector, however, requires a special operator's license and a testing supervisor trained in handling radiation sources (39).

Dichlorodifluoromethane (Freon-12)--A number of commercial companies, as well as the U.S. Government, have developed respirator quantitative fit testing methods using dichlorodifluoromethane as a challenge gas. One representative version of this test, developed by the U.S. Bureau of Mines, is implemented by having the user don a protective mask fitted with a 1/8-in. (0.3175 cm) diameter sampling port. The respirator is fitted with a high-efficiency charcoal cartridge(s) to remove dichlorodifluoromethane from the user's inspired air. The user then enters a chamber containing a stabilized concentration of 1000 ppm dichlorodifluoromethane. Leakage of the respirator face-to-facepiece seal is measured by sampling the air mixture (1.72 liter/min rate) inside the facepiece breathing zone using a sampling pump connected to the respirator sampling probe. The sampled mixture is photometrically analyzed on a Davis-Halide meter, and the output is displayed on a strip-chart recorder. With this scheme, 2 ppm of dichlorodifluoromethane is readily detectable; for a 1000 ppm challenge gas mixture, this represents a measurable leakage of 0.2% (1, 2, 174, 175, 197, 214, 265, 283, 286, 287, 289).

Helium--The Scott Aviation Division of A-T-O Incorporated has developed a respirator quantitative fit test procedure that uses helium as a challenge gas. To implement this test, the user dons a respirator and enters a chamber that has a stabilized air mixture containing a 10% concentration of helium. Breathing oxygen (medical quality) is supplied to the user from a regulated cylinder supply. The user's oxygen consumption rate for the leak test is measured by the drop in cylinder pressure with time. The leakage of helium through the respirator face-to-facepiece seal is measured using a VEECO MS98

mass spectrometer. A small diaphragm-type sampling pump is connected to the 1/8-in. (0.3175 cm) diameter port that has been fitted to the respirator facepiece near the breathing zone. A sampling rate of 300 cm^3/min is used. The helium leak detection method has measured penetrations in the range of 1.0 to 0.001% (36, 175, 284, 286).

n-Pentane--The Federal Aviation Administration, Survival Research Unit, has developed an n-pentane challenge gas respirator quantitative fit test method. To implement this test, an 85-ft^3 exposure chamber is used with a syringe-type infusion pump to establish and control a 120-ppm n-pentane gas concentration. The user dons a respirator that has several small stainless-steel needles (21 gauge by 25 mm long) inserted through the the facepiece. Plastic sampling tubing is attached to each needle. Once inside the test chamber, the user breathes medical-quality oxygen supplied by a demand regulator. The oxygen supply cylinder is positioned on a sensitive high-capacity balance. Oxygen cylinder weight loss is used to compute the oxygen consumed for the duration of the test. Safety precautions must be taken to control the increase of oxygen within the chamber. The nitrogen concentration is monitored continuously with a Med-Science Model 505 Nitralyzer. Cylinders of compressed air are connected through flowmeters to the chamber to provide vent air. The rate of venting is adjusted to compensate for increases in the oxygen concentration. A microvolume rotary selector valve is used to select a sampling port from which a gas sample is drawn and evaluated. A slight negative pressure differential is used to transfer a 50-µl gas sample from the respirator facepiece to a dual-column gas chromatograph with a hydrogen-flame ionization detector (Perkin Elmer Model 800). Operational tests using this leak detection scheme have measured leakages as low as 1.0% (48, 49, 175).

Sulfur Hexafluoride--The Los Alamos Scientific Laboratory has developed a sulfur hexafluoride respirator quantitative fit test method. To implement this test, the user dons a respirator complete with oxygen breathing tubes and is placed inside a test chamber with the atmosphere controlled to sustain a concentration of 50-ppm sulfur hexafluoride in room air. The breathing zone behind the respirator facepiece is sampled through a port and connecting tube. Samples from the test chamber and respirator facepiece port are analyzed with a hydrogen-flame photometer (Meloy Laboratory Sulfur Gas Analyzer). In a hydrogen-rich flame, sulfur emits a characteristic luminescence at the 394 nm wavelength, and the intensity of luminescence is a direct function of the sulfur concentration. This system has a lower detection limit of 0.5-ppm sulfur hexafluoride. Since the chamber concentration is maintained at 50 ppm, the sensitivity of the sulfur hexafluoride RQFT system is 1.0% (147, 149).

Quantitative Aerosol Challenge Agent Fit Test Methods

Di-2-ethylhexyl Phthalate--The Los Alamos Scientific Laboratory has developed a di-2-ethylhexyl phthalate RQFT method. To implement this test, the user dons a respirator that has a sampling port in the facepiece breathing zone and enters a test chamber whose airflow circulation is 2.12 m^3/min. Two aerosol generators are used to produce a 25 mg/m^3 DEHP chamber challenge aerosol concentration. A fan in the test chamber continually mixes the DEHP aerosol and room air; this results in a uniform chamber challenge aerosol concentration of 25 ± 5 mg/m^3. The DEHP aerosol has a mass median aerodynamic

diameter (MMAD) of 0.6 ± 0.2 μm with a geometric standard deviation of 2.00 ± 0.2. A small vacuum pump is used to draw a 1-liter/min sample from the respirator sample port. The amount of DEHP aerosol in a sample is quantified by measuring the intensity of light scattered from the aerosol particles as they pass through a conical scattering chamber using a photomultiplier tube. The concentration of a sample is electronically processed and calculated as a percentage of the chamber challenge concentration, and the result is displayed on a strip-chart recorder. This RQFT method has measured leakages as low as 0.0001% (16, 91, 102, 147, 150, 175, 179, 180, 214, 251, 261, 277, 278, 284, 286, 294).

Sodium Chloride--The sodium chloride RQFT has received considerable attention in the United States and several foreign countries. In the United States, the pioneer organization responsible for developing the sodium chloride RQFT method was the Los Alamos Scientific Laboratory. To implement this test, the user dons a respirator fitted with a sampling port in the facepiece breathing zone and is placed inside a transparent plastic hood which is drawn snugly around the user's waist to minimize leakage to the ambient atmosphere. In the Los Alamos Scientific Laboratory scheme, a solid-particle sodium chloride aerosol is generated by two Wright-design nebulizers mounted in a polyethylene mixing and drying chamber. The nebulizers inject the atomized sodium chloride solution perpendicularly into a drying airstream. The nebulizers can be operated singly or as a pair, depending upon the desired aerosol concentration and flow rate. Air for drying the aerosol is supplied with a two-stage, high-efficiency filtered centrifugal blower. The airflow is measured with an orifice meter and magnehelic pressure gauge and is regulated by the blower's electronic speed control. After passing through the mixing and drying chamber, the liquid sodium chloride droplets form discrete solid particles that are delivered to the top center of the plastic hood (flow rate regulated to 85 liters/min). Directly below the hood inlet is a small circular plate that uniformly distributes the aerosol throughout the test hood. The challenge aerosol in the test hood has a concentration of 15 ± 2 mg/m^3, and the particles have an MMAD of 0.66 ± 0.12 μm with a geometric standard deviation of 2.15 ± 0.19. Excess aerosol is allowed to escape from the hood through the waist seal. Two sampling tubes are connected to the aerosol detection instrumentation. One tube samples the concentration of sodium chloride aerosol in the test hood; this is also used to calibrate the flame photometer. The other tube samples for sodium chloride that has leaked into the respirator breathing zone. A sampling rate of 300 cm^3/min is used. Propane is used for the flame photometer, and it is supplied from an external tank. Analytical grade (99% minimum) propane is used to minimize flame impurity interference. The propane burner and photomultiplier tube assembly is a Baird Atomic model. The photomultiplier tube analyzes the flame through a neutral-density sodium filter which has a peak response at 589.5 nm and a bandwidth of 10 nm at 50% transmission. The output of the photomultiplier tube is electronically processed to calculate the amount of aerosol that has leaked into the respirator facepiece. This information is displayed as a percentage of the ambient hood challenge concentration on a strip-chart recorder. This description of the Los Alamos Scientific Laboratory sodium chloride RQFT method is representative of the other schemes developed in the United States and abroad. In operational use, sodium chloride RQFT systems have demonstrated leakage sensitivities as low as 0.0001% (26, 39, 60, 61, 92, 101, 147, 148, 149, 170, 175, 255, 261, 284, 285, 286, 294).

Bacillus Subtilis/Bacillus Globigii Spores--The U.S. Army has developed an RQFT method that uses a nonpathogenic aerosol of Bacillus subtilis or Bacillus globigii spore-forming bacterium as a challenge agent. To implement this method, a test chamber challenge aerosol environment is created by continuously atomizing a water suspension of bacterial spores using a Binks spray nozzle. An aerosol concentration of 300,000 spores/liter is maintained by dynamically exhausting the test chamber and monitoring the chamber concentration with a Naval Research Laboratory smoke penetration meter. The aerosol can be physically characterized as particles having a mass median diameter of 2.1 μm, and 95% of the particle's diameters fall between 1.0 and 5.0 μm. To implement this test, the user dons a protective mask and enters the test chamber. A specially designed mouth sampler is used to collect the spores penetrating the respirator. The sampler consists of a latex mouthpiece which holds an oval brass cartridge packed with surgical-quality cotton. The cotton serves as the sampling medium for leaked spores; it is packed to a resistance of 25 mm of water at a linear air flow of 10 liters/min. The mouth sampler is positioned in the mouth so that it barely protrudes beyond the lips. When participating in a test, the user inhales through the sampler and exhales through the nose. After the test, the cotton is removed from the brass cartridge with sterile forceps and placed in a bottle containing 25 ml of sterile water and heated for 30 min at 60°C. The sample is then mechanically shaken for 10 min to remove the spores from the cotton. The number of spores in the sample is quantified using standard bacteriological plating procedures. A penetration factor is calculated using the measured sample spore concentration. Accurate quantitation of respirator leakage as small as 1% has been measured (27, 79, 80, 81, 82, 83).

Uranine--The Harvard School of Public Health has developed a uranine aerosol challenge agent RQFT method. Uranine is a commercial dyestuff that is used as a tracer in medical and air pollution work. The disodium salt of fluorescein is readily soluble in water and excited by blue light ranging from 4400 to 5100 Å and emits at 5100 to 5900 Å. To implement this test, the user dons a respirator fitted with a sampling port in the facepiece breathing zone and is placed inside a transparent plastic hood which is drawn snugly around the waist. The challenge aerosol is generated using Pen-I-Sol nebulizer. A 2.35% solution of uranine is placed in the nebulizer. The nebulizer operates with prefiltered compressed air regulated to flow at 3.5 liters/min. The solid aerosol passes through two standard Greenberg-Smith impingers which remove large particles from the stream. Dilution air, which has been dried and filtered, is metered and mixed with the aerosol in a second drying chamber where a 4 mg/m^3 concentration of challenge aerosol is supplied to the test chamber. The geometric mean size of the particles in the challenge aerosol is 0.2 μm with a standard deviation of approximately 2.0. The evaluation of a respirator face-to-facepiece seal is accomplished by simultaneously sampling the test chamber and respirator breathing zone. A Photovolt Multiplier Fluorescence Meter (Model 520M) and Photovolt Fluorescence Unit (Model 54) are used to compare the concentrations of the challenge aerosol measured outside to that measured inside the respirator facepiece. Leakage of challenge aerosol is displayed on a strip-chart recorder. This RQFT method has the capability of detecting leaks as low as 0.05% (25, 27, 221, 284, 286).

COMMERCIALLY AVAILABLE RQFT SYSTEMS

The USAF School of Aerospace Medicine has cataloged descriptive/technical/price information from the three U.S. manufacturers of RQFT systems (39, 261, 294). The three commercial companies, by alphabetical tabulation, are:

1. Air Techniques Incorporated
   1717 Whitehead Road
   Baltimore, Maryland 21207
   Mr. Samuel B. Steinberg, President
   Telephone: (301) 944-6037

2. Dynatech Frontier Corporation
   P.O. Box 30041
   Albuquerque, New Mexico 87110
   Dr. Charles L. Wright, Jr., President
   Telephone: (505) 226-7932

3. National Draeger Incorporated
   Parkway View Drive
   Pittsburgh, Pennsylvania 15205
   Mr. Rolph Dangers, President
   Telephone: (412) 787-1131

Of the three commercial firms marketing RQFT systems, the buyer is limited to the following challenge agents:

1. Gas Test Challenge Agent
   Ethylene - National Draeger Incorporated

2. Solid Aerosol Challenge Agent
   Sodium Chloride - Air Techniques Incorporated and Dynatech Frontier Corporation

3. Liquid Aerosol Challenge Agent
   Di-2-ethylhexyl Phthalate - Air Techniques Incorporated and Dynatech Frontier Corporation

For each RQFT system marketed, most companies offer a complete set of components/instrumentation needed to conduct a fit test. In addition, all offer consumable/replacement parts. Dynatech Frontier Corporation conducts a one-day seminar to train users on equipment operation and a one-day seminar on maintenance. Air Techniques Incorporated offers technical field-service and equipment rental options. All companies advertise their systems are designed to be set up, operated, and, if portable, to be repackaged by one person. For either di-2-ethylhexyl phthalate or sodium chloride RQFT systems offered by Air Techniques Incorporated or the Dynatech Frontier Corporation, all portable units are equipped with a transparent plastic head-to-waist level tent-type challenge aerosol chamber. All semiportable units are fitted with caster wheels and normally use booth-type test chambers. Tables 1, 2, and 3 present the more important characteristics of the RQFT systems available (39, 261, 294).

TABLE 1. AIR TECHNIQUES INCORPORATED

Model	Challenge agent	Detector	Particle size	Chamber/hood challenge agent concentration	Threshold sensitivity	Dynamic range	Recorder	Portability	Unit cost
TDA-50	Di-2-ethylhexyl phthalate (DEHP) aerosol	Forward light scattering photometer	0.7 µm geometric mean diameter	25-100 mg/liter	0.001% (standard) or 0.0001% (optional)	Linear from 100-0.001%	Rack-mounted strip-chart recorder and meter readout	300 lb (136.1 kg) modular cabinet: roll-around type (semi-portable)	$5,250
TDA-60	Sodium chloride aerosol	Flame photometer (propane gas)	0.7-0.8 µm mass median aerodynamic diameter	8-35 mg/liter (approximate)	0.001%	Four ranges: 0-100% 0-10% 0-1% 0-0.1%	Meter readout (standard) strip-chart recorder (optional)	300 lb (136.1 kg) modular cabinet: roll-around type (semi-portable)	$7,300
TDA-80	Di-2-ethylhexyl phthalate (DEHP) aerosol	Forward light scattering photometer	0.45 µm mass median diameter	Adjustable--data not available	0.001%	Five ranges: 0-100% 0-10% 0-1% 0-0.1% 0-0.01%	Meter readout with strip-chart recorder	105 lb (47.7 kg) aluminum locker carrying case; 15-min setup time	$6,500

(Ref 261)

TABLE 2. DYNATECH FRONTIER CORPORATION

Model	Challenge agent	Detector	Particle size	Chamber/hood challenge agent concentration	Threshold sensitivity	Dynamic range	Recorder	Portability	Unit cost
FE 250A	Di-2-ethylhexyl phthalate (DEHP) aerosol	Forward light scattering photometer	0.6 μm mass median aerodynamic diameter	25 mg/m^3 (nominal)	0.0001%	Five ranges: 0-100% 0-10% 0-1% 0-0.1% 0-0.01%	Strip-chart recorder	137 lb (62.2 kg) packaged in three aluminum suitcases	$10,900
FE 257	Di-2-ethylhexyl phthalate (DEHP) aerosol	Forward light scattering photometer	0.5-0.7 μm mass median aerodynamic diameter	25 mg/m^3 (nominal)	0.0001%	Four ranges: 0-100% 0-10% 0-1% 0-0.1%	Strip-chart recorder	100 lb (45.4 kg) packaged in two aluminum suitcases. Table-top model.	$ 7,900

TABLE 2. DYNATECH FRONTIER CORPORATION (continued)

Model	Challenge agent	Detector	Particle size	Chamber/hood challenge agent concentration	Threshold sensitivity	Dynamic range	Recorder	Portability	Unit cost
FE 259	Di-2-ethylhexyl phthalate (DEHP) aerosol	Forward light scattering photometer	0.5-0.6 µm diameter	5-100 mg/m^3	0.0001%	Five ranges: 0-100% 0-10% 0-1% 0-0.1% 0-0.01%	Strip-chart recorder	300 lb (136.1 kg) modular cabinet: roll around type (semi-portable)	$12,260
FE 560	Sodium chloride aerosol	Flame photometer (propane gas)	0.7-0.8 µm diameter	7.5-35 mg/m^3	0.0001%	Five ranges: 0-100% 0-10% 0-1% 0-0.1% 0-0.01%	Strip-chart recorder	325 lb (147.5 kg) modular cabinet: roll around type (semi-portable)	$13,530

(Ref 294)

TABLE 3. NATIONAL DRAEGER INCORPORATED

Model	Challenge agent	Detector	Particle size	Chamber/hood challenge agent concentration	Threshold sensitivity	Dynamic range	Recorder	Portability	Unit cost
Model 80 detector tube version	Ethylene	Draeger developed chemically sensitive detector tube	Gaseous challenge agent	2% volume of ethylene	0.5 ppm ethylene	0.0025-0.05%	Ethylene detector tube	All components packaged in a hand-held box	$300
Model 80 leak detector version[a]	Sulfur hexafluoride	Radioactive ionization detector--electron capture	Gaseous challenge agent	2% volume of sulfur hexafluoride	Data not yet available. Will be better than the detector tube version.	Data not yet available. Will be better than the detector tube version.	Meter readout	All components packaged in a hand-held box	At least $1,000

[a]National Draeger Incorporated has no intention of marketing the Model 80 leak detector version in the United States. (Reference a personal telephone call with Mr. Fleming, Sales Representative, National Draeger Incorporated, 25 July 1979)

(Ref 39)

HUMAN COMPATIBILITY OF RQFT CHALLENGE AGENTS

Although only three U.S. manufacturers market commercially available RQFT systems, and the challenge agents used are di-2-ethylhexyl phthalate (DEHP), ethylene, or sodium chloride, it is still worthwhile to consider relative human compatibility of all agents discussed in this report. The order of analysis will follow that used in the preceding sections that described qualitative and quantitative fit test methods.

Qualitative Fit Test Challenge Agents

Isoamyl Acetate--Isoamyl acetate ($C_7H_{14}O_2$) has a molecular weight of 130.21. Two common synonyms for this substance are banana oil and pear oil. The toxicity dose-data for this substance is summarized in Table 4. The current threshold limit value (TLV) for this substance in air is 100 ppm or 525 mg/m^3.

Stannic Chloride--Stannic chloride ($SnCl_4$) has a molecular weight of 260.49. The toxicity dose-data for this substance is summarized in Table 5. The current TLV for this substance in air is 2 mg $(Sn)/m^3$, and it is corrosive.

Titanium Tetrachloride--Titanium tetrachloride ($TiCl_4$) has a molecular weight of 189.7. The toxicity dose-data for this substance is summarized in Table 6.

There is no published TLV for titanium tetracnloride; however, it is highly corrosive and presents a special hazard because it reacts violently with water to liberate heat and produce hydrochloric acid. Serious injuries have resulted when industrial workers were sprayed with water after being splashed with the chemical. It should be removed from the body by dry wiping before any washing with water is attempted. Burns resulting from its action are deep and slow to heal. A splash of the liquid in an eye may lead to permanent eye structure damage. Immediate wiping of the eyelids and adjacent facial structures with a dry cloth, followed by copious washing of the eye with water, is necessary to avoid severe injury. The main effect of titanium tetrachloride fume on the lungs is corrosive; exposure often results in an intense chemical bronchitis or pneumonia. Fume exposure is treated by breathing pure oxygen to minimize the possibility of developing pulmonary edema. In a limited study of chemical workers who had prolonged exposure to low-level concentrations of the fume, no definite evidence of progressive pulmonary change or dysfunction could be detected (133, 193, 216).

Talcum Powder--Talcum powder is a finely pulverized native hydrous magnesium silicate. Other minerals are almost invariably present in intimate association with talc. The most common ones are chlorite and magnesite, but serpentine minerals, tremolite, anthophylite, dolomite, calcite, and quartz may also be present. Tremolite and anthophylite belong to the amphibole group of asbestos minerals--a fact which has an important bearing on the pathogenesis and pathology of some forms of talc pneumoconiosis. Tremolite talc has been found in some U.S.-produced cosmetic talcum powders.

TABLE 4. ISOAMYL ACETATE TOXICITY DATA

Species tested	Route of exposure or administration	Lowest lethal dose (mg/kg)	Lowest toxic concentration (ppm)	Lowest lethal concentration (mg/m^3)	Lethal dose fifty (LD50) (mg/kg)
Human	Oral	500 (estimate)			
Human	Inhalation		700		
Cat	Inhalation			35,000	
Rabbit	Oral				7,422
Guinea pig	Subcutaneous	5,000			

(Ref 67, 178, 216)

TABLE 5. STANNIC CHLORIDE TOXICITY DATA

Species tested	Route of exposure or administration	Lethal dose fifty (LD50) (mg/kg)	Lowest lethal dose (mg/kg)
Mouse	Intraperitoneal	46	
Dog	Subcutaneous		159
Dog	Intravenous		35
Rat	Oral	700	

(Ref 67, 216)

TABLE 6. TITANIUM TETRACHLORIDE TOXICITY DATA

Species tested	Route of exposure or administration	Lowest lethal concentration (mg/m^3)
Mouse	Inhalation	10

(Ref 216)

No acute toxicity is recognized; however, an individual may suffer mild pneumoconiosis after chronic inhalation, which may progress to pulmonary fibrosis and granulomatosis. A case of this type has been reported in which extreme lesions of the stomach and heart were observed. The current TLV for this substance is 700 million particles-per-cubic-meter (67, 216).

Chloropicrin--Chloropicrin is synonymous with trichloronitromethane; it has use as a fumigant and tracer gas. Chloropicrin vapor is intensely irritating to skin, eyes, mucous membranes, and stomach. Ingestion of the liquid will produce severe gastroenteritis. The molecular weight of this substance is 164.37, and it has a formula of CCl_3NO_2. The toxicity dose-data is summarized in Table 7 (67).

The current TLV of this substance is 0.1 ppm, and it carries a poison label. Finally, this substance is being tested by the National Cancer Institute (NCI) for carcinogenicity by standard bioassay protocol as of April 1976 (216, 264).

Uranine--Uranine [$Na_2(C_{20}H_{10}O_5)$] is a disodium salt of fluorescein, and it has a molecular weight of 376.78. Uranine is a commercial/medical dyestuff. It is a red-orange powder that is readily soluble in water. The therapeutic uses of uranine are based on the fact that the compound is strongly fluorescent (green), appears readily in the extracellular fluids, and gains access to viable cells. The clinical applications of uranine include the diagnosis of eye disorders, the determination of blood circulation time, the adequacy of blood supply, and tissue viability. Practically no toxic effects accompany the intravenous administration of uranine. An occasional patient may experience nausea and vomiting. The toxicity dose-data of this substance is summarized in Table 8.

There is no published TLV for this substance; however, it is on the NIOSH suspected carcinogen list (216, 264).

Quantitative Gaseous Fit Test Challenge Agents

Argon--Argon (Ar) is an inert nonflammable gas whose molecular weight is 39.95; it is a 0.93% constituent of the earth's atmosphere. The only identifiable toxic effect of argon is that it can be a simple asphyxiant. To be

TABLE 7. CHLOROPICRIN TOXICITY DATA

Species tested	Route of exposure or administration	Lowest lethal dose (mg/kg)	Lowest lethal concentration (mg/m^3)	Lowest toxic concentration (mg/m^3)	Lethal dose fifty (LD50) (mg/kg)
Human	Oral	5 (estimate)			
Human	Inhalation		2,400		
Human	Inhalation			2	
Rat	Oral				1,600
Cat	Inhalation		800		
Rabbit	Inhalation		800		
Guinea pig	Inhalation		800		

(Ref 216)

TABLE 8. URANINE TOXICITY DATA

Species tested	Route of exposure or administration	Lethal dose fifty (LD50) (mg/kg)	Lowest toxic dose (mg/kg)	Lowest lethal dose (mg/kg)
Rat	Intraperitoneal	1,700		
Rat	Subcutaneous		17	
Mouse	Intraperitoneal	1,800		
Guinea pig	Intraperitoneal			1,800

(Ref 216)

considered an asphyxiant, argon must compose more than 82% by volume of an individual's breathing air. TLVs are not assigned for a simple asphyxiant because the limiting factor is the amount of available breathing oxygen present (203, 275).

Ethylene--Ethylene (C_2H_4) is a colorless flammable gas with a molecular weight of 28.05. Ethylene is classified as a simple asphyxiant by the American Conference of Governmental Industrial Hygienists (ACGIH) (51). The toxicity dose-data for this gas appears in Table 9.

Dichlorodifluoromethane--Dichlorodifluoromethane (CCl_2F_2) is a nonflammable gas used as a refrigerant and propellant in aerosol bombs. This substance has a molecular weight of 120.91. The most common synonym is Freon-12. A number of investigators have studied the toxic effects of this substance. For animals exposed to an atmospheric concentration of 20% dichlorodifluromethane, 7-8 hours per day for 12 weeks, only mild intoxication and tremors were noted. No gross pathologic alterations or persistent effects were observed. Data for exposures to higher concentrations (80% by volume or more) are difficult to interpret because of the oxygen tensions prevailing in the breathing atmosphere. One fatal case of bronchopneumonia was reported of a man who punctured the freezing coil of a refrigerator containing Freon-12. It is probable that he aspirated the cold concentrated vapor or liquid or was exposed to dangerous degradation products like HCl, Cl_2, HF, F_2, and phosgene. Because high concentrations of this compound are necessary to cause severe toxic symptoms (80% by volume or more), it has been classified as a practically nontoxic gas. The published TLV for Freon-12 is 1000 ppm or 4950 mg/m^3 (2, 11, 51, 67, 130, 142, 202, 216, 264, 275).

Helium--Helium (He) is an inert nonflammable gas with a molecular weight of 4.00. It is a trace component of the earth's atmosphere (less than 1% by volume). The only identifiable toxic effect of helium is that it can be a simple asphyxiant. However, it only becomes an asphyxiant when it comprises more than 82% by volume of the breathing atmosphere (less than 18% oxygen). Under many clinical therapeutic circumstances, breathing mixtures of 80% helium and 20% oxygen are used for patients with respiratory obstructions, as a substitute for nitrogen when breathing at increased ambient pressures, and in a few special applications in anesthesia. One interesting physical property of helium is its low solubility in human body tissue. Thus, helium can be considered a nontoxic gas; it has no published TLV (36, 69, 146, 216, 275).

n-Pentane--n-Pentane (C_5H_{12}) is a flammable gas with a molecular weight of 72.17. There are two TLV's published for n-pentane. NIOSH recommends 1000 ppm and ACGIH recommends 600 ppm or 1800 mg/m^3 (216, 275). The toxicity dose-data for this gas appears in Table 10.

Sulfur Hexafluoride--Sulfur hexafluoride (SF_6) is an odorless, colorless, nonflammable gas whose molecular weight is 146.06. This compound has been reported to be an essentially nontoxic gas. In one experiment. 50 rats were exposed to an atmosphere composed of 80% sulfur hexafluoride and 20% oxygen for periods from 16-24 hr. The rat population showed no ill effects from the exposure. However, the Los Alamos Scientific Laboratory has reported that commercially available sulfur hexafluoride may contain toxic impurities.

TABLE 9. ETHYLENE TOXICITY DATA

Species tested	Route of exposure or administration	Lethal concentration fifty (ppm)	Lowest lethal concentration (ppm)
Mouse	Inhalation	95	
Mammal	Inhalation		95,000 (5-min exposure)

(Ref 216, 275, 293)

TABLE 10. N-PENTANE TOXICITY DATA

Species tested	Route of exposure or administration	Lowest lethal concentration (ppm)	Lowest toxic concentration (ppm)
Human	Inhalation	130,000 (estimate)	
Human	Inhalation		50,000 (5-min exposure)

(Ref 216)

These impurities are sulfur tetrafluoride (SF_4) and sulfur pentafluoride (S_2F_{10}). The TLV for sulfur tetrafluoride is 0.1 ppm, and the TLV for sulfur pentafluoride is 0.025 ppm. The recommended procedure to avoid this potential contamination problem is to purchase the more expensive 99.995% pure sulfur hexafluoride. In the pure form, sulfur hexafluoride is considered to be pharmacologically inactive and can be regarded as a nontoxic gas. The published TLV for SF_6 is 1000 ppm or 6000 mg/m^3 (51, 53, 143, 216, 279).

Quantitative Aerosol Fit Test Challenge Agents

Di-2-ethylhexyl Phthalate--Di-2-ethylhexyl phthalate is an ester of phthalic acid and is widely used in the plastics industry to impart flexibility to rigid polymers (especially PVC) (82, 84, 111, 119, 133, 269). DEHP has the appearance of a colorless oily liquid, and it has a very mild odor. The molecular weight of DEHP is 390.6, and its formula is $C_6H_4[CO_2CH_2CH(C_2H_5)C_4H_9]_2$. DEHP is poorly soluble in water (less than 0.005 ml/100 ml at 25°C), but it is highly soluble in a variety of organic solvents and oils. Of biological significance is the fact that DEHP is soluble in blood and other lipoprotein-containing materials (40, 66, 88, 106, 109, 111, 116, 137, 156, 201.

222, 227, 236, 274, 276, 279). Since there is concern that DEHP may be harmful to humans, this section will review the evidence on the toxicity and possible health hazard this ester presents directly or indirectly to man.

1. Terminology. At times the terminology for the phthalate ester, di-2-ethylhexyl phthalate, is confusing. Most uncertainty has centered around the fact that industry frequently refers to di-2-ethylhexyl phthalate as dioctyl phthalate or DOP. In fact, another member of the phthalic acid ester family, di-n-octyl phthalate, is more appropriately called "dioctyl" phthalate or DOP. In the literature, it is sometimes difficult to be sure which of these two compounds is being discussed. In this report a distinction will be made. Di-2-ethylhexyl phthalate will only be considered synonymous with DEHP.

2. Acute Toxicity. Extensive studies have been accomplished regarding the acute toxicity of DEHP in a variety of experimental animal species. Acute toxicity information in mice and rats was published several decades ago by Hodge (94). Subsequent research by numerous investigators has led to the collation of lethal dose fifty (LD50) data for four species of animals with five routes of administration (oral, intraperitoneal, intravenous, dermal, and inhalation). The results of these studies are summarized in Table 11.

Much of the acute toxicity data pertaining to DEHP requires critical appraisal, particularly with regard to its route of administration, dose and dosing protocols, vehicle used, and rate of administration. It is apparent that DEHP has a low order of toxicity whether it is administered orally, intraperitoneally, or intravenously. Because it is poorly absorbed, DEHP does not, in general, cause irritation when applied to the skin. Studies conducted on the acute inhalation toxicity of DEHP reveal a similar trend. Shaffer et al. (246) exposed rats continuously to a saturated DEHP mist (room temperature; concentration of the inspired air was not reported) and observed no fatalities in 2 hr; however, all exposed rats succumbed after a 4-hr exposure. In another study, Lawrence et al. (131) repeatedly exposed a group of 60 mice (1-hr exposure, 3 times per week) to room temperature air saturated with DEHP vapors (concentration of the inspired air was not reported). Only 1 of the 60 mice died during this study (after 4 weeks of exposure). Under these circumstances, this death was considered unrelated to the DEHP vapor treatment. For all 60 mice, histological examination of the tissues, particularly the lungs, after 4, 8, 12, and 16 weeks of exposure, failed to reveal consistent abnormalities which could be attributed to the inhalation of the DEHP vapor.

3. Subacute and Chronic Toxicity. The subacute and chronic toxicity of DEHP has been investigated in several species of laboratory animals including rats, guinea pigs, and dogs (8, 31, 40, 65, 87, 122, 131, 189, 205, 246). These research efforts generally were involved with oral toxicity studies lasting from 90 days to 2 years in the rat, 1 year in the guinea pig, and about 1 year in the dog.

As early as 1945, Shaffer and associates (246) reported a DEHP subacute toxicity study using rats. DEHP was administered in the daily diet at concentrations of 3.0, 1.5, 0.75, and 0.375% of body weight for 90 days. At the three highest levels, there was a slight decrease in growth compared to control rats, and at the two highest doses, tubular atrophy and degeneration in the testes were observed. However, no abnormal blood disorder was noted with

TABLE 11. ACUTE TOXICITY OF DEHP

Species tested	Route of exposure or administration	Lethal dose fifty (LD50) (g/kg)
Mouse	Oral	13
Mouse	Oral	26
Mouse	Oral	34
Mouse	Oral	49.7
Mouse	Oral	128
Mouse	Intraperitoneal	14.19
Mouse	Intraperitoneal	33.3
Rat	Oral	26
Rat	Oral	30.6
Rat	Oral	34.5
Rat	Intraperitoneal	30.7
Rat	Intraperitoneal	50
Rat	Intravenous	13
Rabbit	Oral	30
Rabbit	Oral	33.9
Rabbit	Dermal	25
Guinea pig	Oral	26.3
Guinea pig	Dermal	10

(Ref 8, 28, 31, 40, 65, 87, 120, 124, 125, 131, 189, 192, 201, 205, 216, 243, 246)

any of the doses. The authors concluded that no injury resulted from the oral administration of 0.2 g/kg per day or less, while a slight retardation in growth occurred at the 0.4 g/kg-per-day dose.

In 1953, Carpenter et al. (31) published a chronic oral toxicity study on DEHP using rats, guinea pigs, and dogs. The rat experiment was designed as follows. Groups composed of 32 male and 32 female Sherman rats constituted

the parental (P_1) generation of rats. These rats were maintained for a maximum of 2 years on diets containing 0.4, 0.13, and 0.04% by weight of DEHP. In addition, approximately 80 first filial generation (F_1) rats were maintained for 1 year on a diet containing 0.4% by weight of DEHP. Appropriate controls for each group received a basal diet without DEHP. The criteria selected for statistical comparison with the untreated controls were mortality, life expectancy, body weight, food consumption, liver and kidney weights, micropathological changes, neoplasm incidence, hematology, and fertility.

DEHP was added to the diet after the animals reached the age of 60 days. Male and female rats on the 0.4% DEHP diet were mated, and pregnant females were isolated until they gave birth and the pups were weaned or died. The pups were removed from the mother after they had reached an age of 15 days, at which time they received a diet similar to the mother's. A portion of the animals in P_1 were sacrificed at the end of 1 year of DEHP feeding and the remainder at the end of the second year. All animals in F_1 were sacrificed at the age of 1 year.

Over the 2-year period, there were a number of deaths in P_1 experimental animals and P_1 controls, but there was no indication that treated animals had higher mortalities than the controls. The majority of deaths were attributed to lung infections. In F_1 groups, treated (0.4% DEHP diet) and nontreated animals had a similar mortality rate during the 1-year study. It was interesting that life expectancy of P_1 groups receiving diets containing 0.4% and 0.13% DEHP exceeded that of the control group.

With the 0.4% DEHP diet, P_1 and F_1 male animals had significantly lower body weights than control animals, while lower dietary dose levels had no effect on weight gain. Food consumption for P_1 and F_1 animals was not significantly different from that of the controls at the end of the first year. Also, at the 0.4% feeding level, mean liver and kidney weights were significantly greater for male P_1 rats after 1 year, while the controls did not differ significantly for any of the other DEHP diet levels.

No tissue or organ patnology was evident which could be attributed to DEHP at any of the levels tested in the P_1 and F_1 groups. No hematologic changes were observed in treated animals which were significantly different from the controls. Fertility did not appear to be altered in treated animals except in the case of F_1 rats at the 0.4% DEHP diet, and this effect was not considered significant by the authors (31).

In a separate study, guinea pigs were administered diets containing 0.13% and 0.4% by weight DEHP for 1 year. No significant differences in deaths, growth, life expectancy, food consumption, liver and kidney weights, and pathology were observed which could be attributed to DEHP. The only unusual effect was that the kidneys of females on the 0.13 and 0.4% diets were larger than those of the controls, but the authors did not consider this as being deleterious (31).

The same investigators also included a 1-year dog study in which the animals were administered, in capsules, 0.03 ml/kg per day, 5 days per week, for the first 19 doses and then 0.06 ml/kg per day until 240 doses were administered. The results of this segment of the study demonstrated that DEHP had no

significant effect on body weight, nor was there any significant difference between liver and kidney weights of treated, untreated, or control animals. One dog in the experiment initially received 0.06 ml/kg for a total of 77 doses and had no ill effects and then received 0.09 ml/kg until an additional 169 doses had been administered. In this dog, fatty vacuolation and limited congestion were observed in the liver, as well as moderate congestion of the kidney. No apparent gross or microscopic pathology of tissues or organs of the dogs was noted with the 0.06 ml/kg dose compared with the controls. The authors concluded that a no-effect dose over a 2-year period fell between 0.06 and 0.2 g/kg per day for rats and 0.06 g/kg per day for the guinea pig and dog (31).

In 1956, Harris et al. (87) published results for a chronic toxicity study of DEHP in rats and dogs. The purpose of this study was to verify the results of the previous studies. DEHP was administered to rats (male and female) in their diets at levels of 0.5% and 0.1% by weight. Groups of animals were sacrificed at 3, 6, 12, and 24 months, and body weights, food consumptions, and organ weights (liver, testes, kidneys, lungs, brain, stomach, heart, and spleen) were studied. Gross and histopathological studies were carried out on selected tissues and organs. Even though mortality of the treated animals was high over the 2-year period, the number of deaths did not differ significantly from those in the control group. After 1 year at the highest dose level (0.5% DEHP), the average weight of the test animals was approximately 50 g less than that of the controls, and in the second year, the average weight of the animals in the 0.5% and 0.1% groups was approximately the same. However, the total number of animals in all groups analyzed was quite small due to deaths and sacrifices during the study. No significant difference was noted in food consumption up to 6 months for the treated animals compared to the controls, but at the end of the first year, food consumption decreased drastically in the 0.5% group with little difference in the 0.1% group. At 6 months, enlarged livers and kidneys were observed in animals on the 0.5% DEHP diet (87).

Two dogs were also used in this study; one was administered 5 g/kg per day for 14 weeks. A no-effect dose of 0.1 g/kg per day was ascertained. In general, the results for rats and dogs were similar for both groups of investigators (31, 87).

Very little information has been published about experimentation with human subjects. Shaffer et al. (246) reported that two adult male volunteers swallowed single doses of 10 cm^3 (equivalent to 144 mg/kg of body weight for a 70-kg individual) and 5 cm^3 of DEHP, respectively. In the first case, this ingestion was accompanied by mild gastric disturbances and moderate catharsis. In the second case, no symptoms whatsoever were noted. In each case, most of the DEHP was excreted in the urine during the 5- to 7-hr interval following dosing, and the remaining 4.5% of the dose was recovered from the urine in the succeeding 24 hours (31, 83, 208, 247).

4. Teratogenicity--Reproduction--Fetal Toxicity. DEHP effects on the reproductive system have been studied by analyzing induced fetal changes. A summary of the experiments and their findings is tabulated in Table 12.

TABLE 12. TERATOGENICITY, REPRODUCTIVE, AND FETAL TOXIC EFFECTS OF DEHP

Species tested	Sex	Route of exposure or administration	Principal finding
Rat	Female	Intraperitoneal	Fetal resorptions, fetal deaths, and decreased fetal size
Rat	Female	Intraperitoneal	Adverse effect upon implantation and parturition; excessive hemorrhaging and fetal retention
Rat	Female	Intraperitoneal	Reduced conception and increased fetal deaths
Mouse	Male	Intraperitoneal	Early fetal death and semi-sterility
Rat	Female	Oral	No effect upon fertility
Rat	Female	Oral	Decreased fetal weight and increased fetal resorptions
Rat	Male	Oral	Testicular degeneration
Ferret	Male	Oral	Testicular degeneration
Rat	Female	Intravenous	No teratogenic or embryotoxic effects

(Ref 31, 50, 64, 122, 124, 125, 146, 189, 204, 205, 207, 234, 245, 246, 247, 248, 249, 250, 268, 280).

Studies using in vitro cell systems reveal that DEHP is cytotoxic to cultured embryonic cells at a concentration of 0.05 mg/ml (135). The developing chick embryo system has been used to examine the effects of DEHP by several investigators. These studies indicate that DEHP possesses an intermediate order of embryotoxicity when compared to other substances, including other phthalic acid esters (18, 47, 134, 135, 136, 204, 274).

In 1945, Shaffer et al. (246) used a 90-day feeding period with rats on diets containing varying amounts of DEHP (typically 1.5% to 3% of body weight), and the results revealed tubular atrophy and degeneration in male rat testes. It was considered noteworthy that in rats, phthalic anhydride severely lowered the testicular ascorbic acid, dehydroascorbic acid, and impaired sperm motility (274). Recently, Seth et al. (245) examined the effects of DEHP on rat gonads and reported that the activities of succinic dehydrogenase

and adenosine triphosphate were significantly reduced, but that B-glucuronidase activity was increased in rat gonads after intraperitoneal treatment with 5 ml/kg of pure undiluted DEHP. Histopathological studies revealed focal degeneration of seminiferous tubules and edema of interstitium in the testes of DEHP-treated rats. In the ferret, orally administered DEHP (1.0% by weight in the diet for 14 months) led to histological changes in the testes, as evidenced by the presence of sterile tubules (124). Tankara et al. (268) reported that the rat testes had low levels of radioactivity after administering [^{14}C] DEHP orally or intravenously.

A comparison of litters born, number of pups, and stillborn pups revealed no difference in rats fed DEHP compared to those animals in appropriate control groups (31). On the other hand, studies in the rat revealed that DEHP caused fetal resorptions and led to deleterious effects upon implantation and parturition (50, 248, 250, 281, 286). Singh et al. (248-250) reported that DEHP (5 and 10 ml/kg, intraperitoneally) on days 5, 10, and 15 of gestation did not interfere with fertility, as evidenced by the ratio of corpora lutea to implantation sites.

In addition, Singh et al. (249) revealed that DEHP, when administered intraperitoneally to male mice, induced fetal or embryonic toxicity in females, who were subsequently mated by these same males, because a higher incidence of resorptions was observed compared to female controls. They reported that DEHP produced a dose- and time-dependent antifertility effect. Also, Nikonorow et al. (189) reported that an oral dose of DEHP (1.7 g/kg per day) to rats led to a significant reduction in placental weights. Both investigators concluded that the effects of orally administered DEHP on reproduction and fetal development were dose-dependent and related to the duration of administration (189, 248, 250, 274).

Garvin et al. (64) evaluated the teratogenic potential of plasma-soluble extracts of polyvinyl chloride (PVC) in rats. Using two different PVC formulations and extracting sterile rat plasma (4°C for 21 days) resulted in a plasma concentration of 85 µg DEHP/ml. When the extracted DEHP was injected intravenously into groups of pregnant rats from day 6 to day 15 of gestation at doses of 1 and 3.7 mg/kg, no differences were observed in growth rates of the mothers, litter size, pup weights, or incidence of dead or resorbed fetuses. There was no evidence of teratogenic or embryotoxic effects in pups from mothers injected with the DEHP. Garvin's findings suggest that the concentrations of DEHP leached from plastic pose no teratogenic problem and that only very high doses seem to cause changes in the reproductive system of experimental animals.

Only one human study concerning the teratogenicity of DEHP could be found in the literature. In this study, Thiess et al. (272) observed a group of 101 workers employed in a BASF DEHP manufacturing plant. The average exposure duration for each worker was 12 years (duration of exposure ranged from 4 months to 35 years). The working place atmospheric concentration of DEHP ranged from 0.0006 to 0.01 ppm. Health hazards caused by DEHP could not be found. There was no evidence of a higher rate of miscarriages or deformities among the female employees or the wives of the male employees. The rate of absenteeism and accidents was not statistically different from BASF as a whole. Also, small quantities of DEHP were found in blood and urine samples of control and exposed groups.

5. Carcinogenicity and Mutagenicity. Krauskopf (122) studied various phthalic acid esters and reported there was no evidence that the phthalates were carcinogenic. No animal data has yet demonstrated that any of the phthalate esters act as carcinogenic agents. Likewise, their role as possible co-carcinogens has not been established (8, 10, 40, 205, 274). While certain commercial polymer films have reportedly caused fibrosarcomas and other tumors in rats, this has been attributed to the physical form (solid versus perforated film) of the material rather than to the polymer or an additive (8, 40, 50, 122, 205, 274). Perhaps the question of carcinogenicity will be answered in a study now in progress by the National Cancer Institute. All the phthalate esters have been identified in the NIOSH Suspected Carcinogen List (1976) for priority attention as a point source water effluent discharge toxic pollutant (264).

Very little published information is available on the mutagenic effects of DEHP. In one study, Singh and associates (249) used mice and the dominant lethal assay test to study the mutagenic effects of DEHP. These authors have reported a decrease of implants and number of live fetuses. In this study, a single dose of undiluted DEHP was intraperitoneally administered to male mice immediately prior to the initiation of a mating period in which 10 treated males were mated (2 females per male) each week for 12 weeks. The dose levels employed were 0.33, 0.5, and 0.66 of the acute LD50 dose. A parallel untreated mating group was maintained as a control (240 matings). Shortly before expected parturition, the pregnant females were sacrificed and the uterine horns exposed surgically to permit recording of the numbers of corpora lutea, total number of implantations, preimplantation losses, resorption sites, dead fetuses, and viable fetuses. Since there was a significant antifertility effect of DEHP, only total fetal deaths were used in the statistical test for dominant lethality. The results, therefore, are a conservative estimate of dominant lethal effects since some of the preimplantation losses may have been due to dominant lethal mutation. The reduction in mean live fetuses per pregnancy and mean implants per pregnancy at the high dose levels of DEHP was consistent with the finding of a significant level dominant lethal mutation for DEHP. Mean implants per pregnancy and mutagenic effects tended to be bimodally distributed in this experiment. The results for this study are presented in Table 13.

Only two studies regarding the mutagenic effects of DEHP were found concerning humans. In one study, Stenchever et al. (262) exposed human fetal lung and leukocyte cells to DEHP at various concentrations and analyzed their chromosomes for possible changes. Fetal lung cells and leukocyte cultures were exposed to 60.0, 6.0, and 0.06 µg/ml concentrations of DEHP. Since isochromatid and chromatid breaks and gaps were a minimum for all doses, they were combined for statistical purposes. In the final analysis, no statistically significant differences were seen between the DEHP-treated cells and the control cells for both fetal lung and leukocyte species.

In the other human study, a German researcher reported that, in comparison to a control group of 20 employees, no evidence of an increased rate of chromosome aberration could be found in a group of 10 plant employees who had been exposed (10-30 years duration) to DEHP. The levels of DEHP vapor concentration ranged from 0.0006 to 0.01 ppm (270).

TABLE 13. MUTAGENIC EFFECTS OF DEHP

Dose (ml/kg)	Pregnancies (percent of control)	Implants	Fetal deaths	Live fetuses
12.78	56	11.3	0.80[b]	10.5
19.17	59	11.1	0.65[c]	10.5
25.56	22	10.5[a]	0.79[b]	9.6[b]
Untreated control	71	11.4	0.45	11.0

[a] Per pregnancy; mean values.
[b] Greater than 99% confidence (Student T-test).
[c] Greater than 95% confidence (Student T-test).
(Ref 249)

Nevertheless, many authors have expressed an opinion that additional studies are needed to confirm these observations and provide clarification of the mutagenic effects of DEHP in humans (8, 50, 113, 122, 274).

6. Absorption. Numerous studies with laboratory animals have revealed that phthalate esters can be absorbed from the gastrointestinal tract, the intraperitoneal cavity, and the lungs. Absorption studies of DEHP have been conducted using a variety of vehicles and dosage protocols.

Schulz and Rubin (241) found that following oral administration of [^{14}C] DEHP (in corn oil) to rats, 13% of the administered dose was recoverable in organic solvent extracts from the urine, feces, and contents of the large intestine, and 62% could be recovered in water extracts. Only negligible amounts of radioactivity were found in major organs. These authors also reported that metabolism of DEHP was extensive, and the rate of metabolism was more rapid than the rate at which it was absorbed from the gastrointestinal tract of the rat (241). In another study, Daniel and Bratt (41) used labelled DEHP in rats and reported that 42% of the radioactivity was eliminated in the feces after 7 days. A significant portion (14%) of the radioactivity was found in the bile. In 1974, Wallin et al. (282) conducted an orally-administered labelled DEHP absorption study on rats and dogs. They reported that 10% less radioactivity appeared in the urine at the 24-hour posttreatment point for the dog relative to the rat. They concluded that a species difference might account for the differences in absorption and/or biliary excretion of DEHP.

7. Distribution. Several studies have reported on the distribution of DEHP following either a single intravenous or oral administration. Most of these studies have used a fixed dose level with a relatively short postinjection time interval and have not really approached the question of accumulation. A major shortcoming with many of these studies has been a suitable vehicle to solubilize the DEHP. Recent studies by Stern et al. (263) have stressed the importance of the physiochemical properties of DEHP in biological systems. Many emulsifying agents, including oleic acid, albumin, Tweens, acacia, corn oil, and serum have been used in distribution studies involving

the rat or mouse. The particular vehicle employed indeed influences the distribution of DEHP. Table 14 summarizes the data to support this conclusion.

Thus, there is little doubt that DEHP can be widely distributed in a variety of tissues following oral or intravenous administration. Distribution studies performed in animals, using various solubilizing agents, indicate a longer retention of the compound without any tendency for accumulation. The rapid metabolism and excretion observed following administration of plasma-solubilized DEHP in both transfused and nontransfused patients suggests there are other sources of the plasticizer to which man is exposed. The phthalate esters are used in a wide variety of products and are known to occur in water, air, and soil throughout the world. Some evidence indicates phthalates occur naturally as a result of biosynthesis (8, 41, 64, 66, 70, 83, 106, 108, 109, 111, 116, 156, 160, 182, 205, 211, 222, 227, 241, 242, 243, 247, 259, 274, 276, 279, 281, 288).

8. Metabolism and Excretion. It is known that DEHP is metabolized after its oral or intravenous administration to experimental animals (4, 41, 224, 241). Following the oral administration of DEHP to rats, Albro et al. (4) were able to isolate four major metabolites of DEHP which were derived from ω and (ω-1) oxidation of mono-ethyl-hexyl phthalate (MEHP) without any attachment on the aromatic ring. The alcohol and ketone derived were not conjugated, and free phthalic acid amounted to less than 3% of the urinary metabolites.

Daniel and Bratt (41) reported the presence of urinary phthalic acid and other metabolites resulting from the oxidation of MEHP. Analysis of rat urine for diets containing [^{14}C] DEHP revealed no MEHP, but did reveal various derivatives of MEHP. Upon hydrolysis, the urine yielded only [^{14}C] phthalic acid. When labelled phthalic acid was administered orally (3.3-40 mg/kg) to rats, it was neither appreciably metabolized nor retained in tissues (288).

Metabolic studies of DEHP have not received much attention. However, one report indicates some degree of biotransformation. Jaeger and Rubin (107) studied urinary phthalate concentrations in a patient who was to undergo open-heart surgery. Before surgery, which involved transfusion of blood containing DEHP, the concentration of urinary phthalic acid was transiently elevated. Urinary phthalic acid content after surgery returned to pretransfusion levels in about 1 day and remained at this level during the 5-day postoperative monitoring period.

Liver perfusion studies have also provided some insight into the metabolism of DEHP. The isolated perfuse rat liver is capable of clearing added DEHP from the perfusion medium within 60 min after its addition. The DEHP was accumulated by the liver in an unmetabolized form (111). Subsequent studies by these investigators using perfused rat liver indicated that within 30 min after perfusion, 90% of the total DEHP contained in the perfusate phase of the system had disappeared, while in the remaining 4 hr an additional 9% was lost. At the end of 4.5 hr, the perfusate was essentially cleared of DEHP. Almost all of the DEHP was recovered from the liver, and there was no trace of phthalic acid in the perfusate (108).

TABLE 14. DISTRIBUTION OF LABELLED DEHP IN SELECTED TISSUES (Relative Concentrations)

Species tested	Route of exposure or administration	Dose	DEHP vehicle	Liver	Lung	Spleen	Fat	Kidney	Heart	CNS	Gonads
Mouse	Intravenous	115 mg/kg	Serum	High	Low	Low	Low	High	Low	Low	Low
Rat	Intravenous	600 mg/kg	Oleic acid	High	High	Low	Low				
Rat	Intravenous	40 mg/rat	Not specified	Moderate	High	Moderate	Low	Low	Low	Low	Low
Rat	Intravenous	800 mg/kg	Not specified	High	____	____	High	High			Low
Rat	Oral	0.1% of diet	Fat	Low	____	____	High	___	Moderate	___	___
Rat	Oral	1000 ppm	Corn oil	High	____	____	High	___	Low	Low	___
Neonate	Intravenous	0.04-1.4 mg	Blood transfusion	____[a]	____	____	____	___	Moderate	___	___
Man	Intravenous	14-600 mg	Blood transfusion	High	Variable	Variable	Variable	___	____	___	___

[a]Specific tissue not measured

(Ref 41, 93, 108, 241, 242, 259, 274, 281, 288)

A series of in vitro studies revealed that rat liver homogenates were unable to hydrolyze DEHP. However, DEHP was rapidly hydrolyzed when incubated with pancreatic lipase. No phthalic acid was detected when either DEHP or MEHP was incubated with pancreatic lipase. A small amount of MEHP was produced by the nonenzymatic hydrolysis of DEHP (41).

Albro et al. (3, 4) have made an extensive survey of DEHP hydrolase activity in various tissue lipases. While such activity can be detected in several tissues, the pancreas, liver, and intestinal mucosa appeared to contain the bulk of DEHP hydrolase. Rat pancreatic DEHP hydrolase can hydrolyze MEHP at about 2% of its DEHP rate. DEHP is extensively metabolized in man and animals. Excretion of metabolites of DEHP occurs mainly through the urine and bile, and there is no conclusive evidence suggesting retention of these compounds in tissues. An intravenous dose of 0.1 mg/kg of DEHP in rats can be nearly totally accounted for within 24 hr after its administration. Following an oral administration of DEHP (200 mg/kg in corn oil), approximately 90% of the dose was recovered after 24 hr, with 55% of the radioactivity detected in the urine and about 35% in the feces (241).

Kinetic studies on the disappearance of organic extractable radioactivity in blood obtained after intravenous administration of [^{14}C] DEHP to rats indicated an elimination half-life of 21 min. The disposition half-life of radioactive, ^{14}C-labelled DEHP emulsion was 263 min in rats following intravenous administration, 83 min for plasma containing polysorbate emulsion, 181 min for plasma containing ethanol, and 31 min for plasticizer (DEHP) leached from plastic bag material into the plasma (107, 227, 241, 276).

In summary, the pharmacokinetic activity in humans and laboratory animals indicates that DEHP is absorbed from the gastrointestinal tract and can be widely distributed in a variety of tissues following oral or intravenous routes of administration. It is rapidly metabolized to a number of derivatives which are excreted primarily in the urine. DEHP has a short elimination half-life and does not appear to accumulate in tissues following transfusion of blood stored in PVC bags.

9. Conclusion. While much has been learned about the effects of DEHP on biological systems during the past 30 years, there is still a paucity of specific toxicological information. It is evident that DEHP-induced toxic effects occur almost exclusively when it is injected in large doses and not when it is administered in the diet or in amounts comparable to those present in blood bag assemblies. Although it is apparent that DEHP is not devoid of biological activity, the manner and level of dosing required to elicit a response make it impossible to establish the significance of such studies for humans. Evidence has been presented to indicate that the toxicity of DEHP, at least under certain circumstances, is dependent upon the physical properties of the preparation. It is not known if DEHP absorbed via the respiratory route is metabolized in the same way as oral or intravenous administration. Metabolism via respiration merits further scientific investigation since RQFT involves this route of exposure.

DEHP is poorly soluble in water, disappears rapidly from the blood, undergoes some degree of biotransformation, and is excreted by the kidney quite rapidly. There is little evidence of any substantial accumulation of DEHP in tissues.

Animal experiments using high doses of DEHP reveal some deleterious effects upon the reproductive system, but there is no evidence that suggests DEHP is carcinogenic. Further investigations are needed to establish the complete toxicological profile of DEHP.

The current NIOSH and ACGIH recommended TLV for DEHP in air is 5.0 mg/m^3 (264, 275).

With respect to DEHP RQFT, it is beneficial to analyze the worst possible human test subject exposure. The following conditions are assumed:

1. DEHP chamber aerosol concentration of 25 mg/m^3.
2. Duration of human exposure is 30 min (actual RQFT is normally 15 min).
3. Human subject inhales an average of 0.72 liters of air per breath; average respiration rate is 15 breaths per min.
4. Human subject will be removed from the test chamber if it is found that the concentration of DEHP aerosol in the respirator facepiece is 10% of the challenge chamber concentration.
5. Complete retention of all DEHP aerosol in the lungs and complete absorption into the bloodstream.

These conditions imply that in a 30-min test period, the human test subject will inhale 324 liters of air (0.72 liters of air per breath x 15 breaths per minute x 30 min). Considering a maximum leakage of 10%, a test subject would thus absorb 810 µg of DEHP, as shown by the following calculation:

$$\frac{2.5\times10^{-3}\ g}{1\ m^3} \times \frac{1\ m^3}{10^6\ cm^3} \times \frac{1\ cm^3}{10^{-3}\ liter} \times \frac{10}{100}\ (leakage) \times 324\ liters$$

This amount is greater than would actually occur because of assumed high respirator leakage, no loss or cleaning of the lung during exhalation, and complete absorption into the bloodstream. Further, this quantity of absorbed DEHP represents an 11.6 µg/kg dose for a 70-kg subject (810×10^{-6} g/70 kg), which is far less than any published toxic dose.

Sodium Chloride--Sodium chloride (NaCl) has a molecular weight of 58.4. The most common synonym is salt. The toxicity dose-data of sodium chloride is summarized in Table 15.

From this data it is obvious that the acute and chronic toxicity of salt is very low. To put this information into a better perspective, the normal daily intake of sodium chloride by an adult is 10-12 g (approximately 160 mg/kg for a 70-kg man) (38). The areas of controversy concerning sodium chloride are focused on its potential link to hypertension, its teratogenic hazard, and its carcinogenic properties.

TABLE 15. SODIUM CHLORIDE TOXICITY DATA

Species tested	Route of exposure or administration	Lethal dose fifty (LD50) (mg/kg)	Lowest toxic dose (mg/kg)	Lowest lethal dose (mg/kg)
Mouse	Oral	4,000		
Mouse	Intraperitoneal	2,602		
Mouse	Parenteral		1,900	
Rat	Oral	3,000		
Rat	Subcutaneous			3,500
Hamster	Oral			500
Guinea pig	Intravenous			2,910
Rabbit	Intravenous			1,110
Dog	Intraperitoneal			364
Dog	Intravenous			2,000

(Ref 20, 21, 37, 67, 74, 120, 121, 153, 166, 167, 216, 218, 236, 264)

The inducement of hypertension by increased sodium chloride consumption has been reported in the rat, rabbit, and chicken (119, 141, 166, 167, 235). Meneely et al. (165-167) observed hypertension in rats chronically fed diets rich in sodium chloride. Some of the animals developed severe renal disease associated with massive edema and a nephritic syndrome. In another chronic study, it was shown that rats which drink 1% saline over a long period of time frequently develop hypertension, generalized vascular lesions, and renal damage (119). However, an experiment by Gross (75) indicated no clear-cut increase in the frequency of hypertension when rats ingested excess sodium chloride. Also, when Wilhelmj et al. (287) tested dogs, they reported that sustained hypertension could not be produced by the ingestion of excess salt. These results were explained by the fact that the dog kidney has a phenomenal ability to eliminate excess salt (287, 289). With respect to the human

species, two reports present a similar conclusion. Grant and Reischsman (71) reported that the daily addition of 20-30 g of sodium chloride to the diet of normal adults does not cause any significant change in the arterial pressure. Similarly, Dahl and Love (30) presented the conclusion from a human study that, while necessary, sodium chloride is not of itself sufficient for the development of hypertension.

Teratogenic effects of sodium chloride in mice have been reported by Nishimura and Miyamoto (191). In this experiment, a single subcutaneous injection of sodium chloride into pregnant mice at the level of 2,500 mg/kg at 10 or 11 days of gestation produced embryocidal, growth-suppressing, and teratogenic effects in the fetuses. Similar treatment at the level of 1,900 mg/kg at 10 days of gestation caused teratogenic effects, and at 11 days of gestation, embryocidal effects. Gross malformations consisted of shortness of the forelimb and foot, malformed wrists and ankle joints, and various digital defects.

No animal experiments have been published showing sodium chloride to be carcinogenic. However, sodium chloride is currently listed in the NIOSH Suspected Carcinogens List. A NIOSH-sponsored investigation is being performed at the National Cancer Institute using standard bioassay protocol (effective April 1976) (69).

Perhaps most important to this report and RQFT is the potential health hazard(s) associated with breathing sodium chloride aerosol. The therapeutic value of enhanced secretion clearance from human lungs after administration of normal and hyperonic saline aerosol is well documented in the literature (14, 62, 99, 115, 163, 173, 198, 199, 203, 229, 230, 231, 233). For example, Pavia et al. (203) used the radioaerosol method to measure the effect of saline aerosol on the rate of secretion clearance from the lung. Two trial runs (a control run and a saline run) were done in each of 7 patients with chronic obstructive lung disease. In both runs, [^{99}Tc] labelled polystyrene particles (5.0 ± 0.7 μm in diameter) were inhaled under controlled conditions by the patients, and their subsequent clearance was monitored for 6 hr by whole lung counters. Scanning was also done with a gamma rectilinear scanner. The saline run was identical to the control run except that 30 min after inhaling the radioaerosol, the patients inhaled an aerosol of hypertonic (1.21 molal) saline for 11 min from an ultrasonic nebulizer. Although the initial distribution of the radioaerosol along the airways was the same in both runs, whole lung clearance during the first 50 min was twice as fast after the inhalation of the hypertonic saline aerosol as in the control. The mean weight of sputum produced was statistically higher in the saline run. The number of coughs in the two runs was the same.

A topic closely related to breathing sodium chloride aerosol is its deposition and retention characteristics in the respiratory tract. In general, during respiration, airborne solid or liquid particles are introduced into the lungs where they settle at different levels; the location of impact depends upon particle size. Coarser particles (3-5 μm in diameter) are deposited on the bronchial tree membranes from which they are normally expelled. The finest particles penetrate further down the lung, and when less than 1 μm in diameter, they may reach the subbronchial parts of the lung (5, 42, 43, 44, 45, 54, 127, 128, 129, 177, 290, 291, 292).

In two previous papers, Dautrebande et al. (43, 44) reported on the behavior of water-insoluble particles. It was shown that relative humidity had no influence upon size and, therefore, upon the site of their deposition. When the particles were hygroscopic, however, the size as measured by optical or electron microscope was not necessarily the deposition size they would be in the lungs. Since the air in the lungs is nearly saturated with water vapor (99.6%), it is clear that particles sensitive to humidity will be affected and, therefore, increase in size immediately after reaching the nostril or the trachea. Sodium chloride, in particular, possesses very interesting hygroscopic properties that impact RQFT (42, 43, 44, 45, 290, 291, 292).

It has been established that in an atmosphere with a relative humidity below 76%, sodium chloride particles exist as fine crystals; above 76% relative humidity, water vapor begins to condense onto the crystal surface, and when the relative humidity increases further, the airborne salt particles exist only in the air as droplets (42, 45). Although the size of the droplets depends upon the relative humidity, it is known that no significant change in the diameter of the droplets takes place before the relative humidity is 90% or above (172). The increase in volume of sodium chloride droplets in a wet atmosphere is particularly marked above 95% relative humidity. Furthermore, between 95% and 99.5% relative humidity, the difference in diameter of the droplets is striking. For example, a sodium chloride particle 1 μm in diameter when dry, increases its diameter only three times at 99% relative humidity, while at 99.5% relative humidity, its diameter increases sevenfold (45).

This enlargement takes some finite time to attain its maximum and depends upon the initial crystal diameter. However, the finest crystals (with diameter below 0.5 μm) need only a small fraction of a second (typically 0.5 sec) to undergo a sevenfold enlargement, a time interval extremely short compared with the duration of their passage through the respiratory tract (42).

It has been reported that the mass retentions of polydispersed aerosols, using 10% saline solution, are 38%, 59%, and 70%, for respiratory rates of 30, 15, and 7.5 per min, respectively. No significant difference was found for tidal volumes of 500 or 1,000 ml (42). Also, for 1% saline solutions, the mass retentions of polydispersed aerosols are reported to be 17% and 35%, for respiratory rates of 15 and 7.5 per min, respectively; again, the tidal volume being either 500 or 1,000 ml (42).

The American Conference of Governmental Industrial Hygienists recommend that the concentration of sodium chloride particles in breathing air be less than 30 million particles-per-cubic-foot (mppcf) or 10 mg/m^3. Any concentration of sodium chloride particles (diameters less than 1 μm) exceeding this recommended concentration would be considered a nuisance particle (275).

Bacillus Subtilis/Bacillus Globigii--Bacillus subtilis/bacillus globigii are spores of a nonpathogenic bacterium. The spore is oval in shape with a particle size of approximately 0.8 μm by 1.2 μm, and when cultured on nutrient agar, forms an orange-pigmented colony. These spores are obtained by growing the organism in a shake culture, centrifuging, washing, resuspending in sterile water, and then heat shocking at 60°C for 30 min which results in a suspension free of viable vegetative cells. Such a stock suspension can be

stored for as long as 6 months at 4°C without any significant change in viable count or colonial characteristics (79, 80, 81, 82, 83).

FINAL RECOMMENDATION OF AN RQFT SYSTEM

Quantitative measurement of facepiece leakage and overall respirator performance can now be accomplished with commercially available equipment by testing subjects wearing the protective mask in simulated working conditions. The protection factor (PF) is calculated by dividing the average ambient challenge agent concentration by the average concentration of the challenge agent measured inside the respirator facepiece. Ideally, the challenge agent should be nonflammable, and the detection method should be capable of following rapid changes in the concentration of the challenge agent with the user's respiratory cycle. A variety of challenge agents and detection methods have been discussed in this report. However, many of the challenge agents are toxic and/or flammable and analytical methods in some cases are neither sufficiently sensitive nor responsive to accurately measure rapidly changing leaks. The Aerospace Medical Division judges argon, helium, DEHP, and sodium chloride, with their associated detection schemes, to be the best options at this time for RQFT. However, because the Occupational Safety and Health Administration (OSHA) has the pressing requirement to quantitatively fit their compliance officers with respirators, the selection of a challenge agent and detection method must be limited to the two commercially available options: DEHP and sodium chloride. Of the two methods, the Aerospace Medical Division recommends DEHP RQFT as the optimal choice. The USAF Surgeon General has also endorsed the use of DEHP RQFT. In the original Statement of Work (SOW), OSHA requested several factors be considered in the final selection of a challenge agent and detection method. Table 16 presents a matrix comparison of the two alternatives with the associated selection criteria used to make a recommendation.

RESPIRATOR QUANTITATIVE FIT TEST PROCEDURE

Except for manufacturer's required procedures peculiar to instrumentation operation, RQFT procedures are practically identical. The following is a suggested procedure:

Qualitative Fit Test

The user dons the respirator according to the manufacturer's instructions. The test is designed to mimic the work environment, so the operator must be assured that the headstraps are not over-tightened to the point of discomfort. If the user wears eyeglasses or safety glasses in the work area, the operator should ensure they are worn with the respirator.

TABLE 16. COMPARISON OF DEHP AND SODIUM CHLORIDE VERSUS SELECTION CRITERIA

Selection criteria	DEHP	Sodium chloride
Challenge agent ambient concentration	25-100 mg/m^3	7-35 mg/m^3
Particle size	0.5-0.6 μm MMAD	0.7-08 μm MMAD
Detector technology	Light-scattering photometer	Propane flame photometer
Sensitivity	0.0001%	0.0001%
Dynamic range	0-100% 0-10% 0-1% 0-0.1% 0-0.01%	0-100% 0-10% 0-1% 0-0.1% 0-0.01%
Display	Strip-chart recorder	Strip-chart recorder
Economy	$5,250 to $12,260	$7,300 to $13,530
Portability	See Notes 1 and 2	See Note 2
Maintenance/logistics	See Note 3	See Note 3
Facility requirements	1) Standard 115-120 volts a.c. power 2) Plant/facility compressed air source can be used if desired	1) Same as for DEHP 2) Same as for DEHP
Special accessories desirable	None necessary	See Note 4
Human compatibility	See Note 5	See Note 6

Note 1. Each manufacturer offers units that can be packed in one or three aluminum cases to facilitate transportability by auto or plane. Net weight approximately 100-140 lb (45.4-63.4 kg).

2. Each manufacturer offers a semi-portable unit that resembles a four-drawer filing cabinet on caster wheels. Net weight 300-325 lb (136.1-147.5 kg).

Note 3. Each manufacturer stocks spare parts for all models. One manufacturer sponsors a 1-day maintenance course on their equipment.

4. A dehumidifier is a highly desirable option if the unit will be operated where the relative humidity exceeds 55%.

5. Although the toxicology information is incomplete to absolutely guarantee human compatibility, the concentration of DEHP used in this testing is judged by the Aerospace Medical Division to be safe for human use. DEHP is poorly soluble in water and the inhaled challenge agent should not be absorbed in the lungs.

6. The only reservation the Aerospace Medical Division has with sodium chloride is the remote possibility of aggravating a case of hypertension. Thus, sodium chloride should not be used with subjects having hypertension or on a sodium-restricted diet. Because sodium chloride is readily retained and absorbed in the lungs, a correction must be made for this property of the challenge agent. This correction can be accomplished by having the user breath a 0.01% sodium chloride aerosol concentration while wearing a half-face respirator equipped with an inlet and outlet port. The test aerosol is delivered to the inlet port and the outlet port is used to sample the exhaled breath. The concentration of sodium chloride in the inspired and expired gases is measured by alternately sampling the inlet and outlet ports. Using this data, a respiratory retention factor (RRF) is calculated as the ratio of the concentration of sodium chloride in the expired gas to that of the inspired gas. An RRF should be calculated for each exercise used in the RQFT procedure. To calculate the corrected protection factor given by an RQFT procedure, multiply each exercise derived PF by the corresponding RRF. The final PF is the average of the corrected exercise PFs (63).

Quantitative Fit Test

Once the operator has determined that the respirator is being worn properly, the fit should be checked using a qualitative fit test. The Aerospace Medical Division recommends using the positive and negative pressure test along with the isoamyl acetate test described earlier in this report. Only after the best possible fit is obtained with qualitative testing, should quantitative testing be initiated.

After the equipment has been calibrated according to manufacturer's instructions, the operator must ensure that a safe concentration of challenge agent has reached equilibrium in the test chamber. Before the user enters the test chamber, the operator will explain the sequence of exercises that are to follow. To minimize respirator filter leakage, high-efficiency particulate filters should be used with the aerosol challenge agent. After the user enters the test chamber, the operator will recheck the instrumentation calibration and chamber concentration.

In response to verbal instructions or those printed on poster boards, the user will be directed through the following set of eight exercises:

1. Normal Breathing (NB). The user stands in a relaxed position with head motionless and arms at the sides. Duration of this exercise will be 1-2 min.

2. Deep Breathing (DB). Standing as described above, the user simulates deep breathing that accompanies hard work. This exercise should be limited to 15-30 sec to prevent hyperventilation.

3. Turning Head Slowly Side-to-Side (THSS). Standing as described above, the user turns the head slowly from side-to-side while breathing normally, pausing for at least two breaths before changing direction. Duration of this exercise will be 1-2 min.

4. Moving Head Slowly Up-and-Down (MHUD). Standing as described above, the user slowly moves the head up and down while breathing normally, pausing for at least two breaths before changing direction.

5. Talking (TK). Standing as described above with the head motionless, the user reads slowly from a prepared text or recites the alphabet. The operator should be able to hear the user. Duration of this exercise will be 1 min.

6. Cough (C). Standing as described above, the user should cough at least twice; the time interval between coughs should be at least 10-15 seconds.

7. Smile (SM). Standing as described above, the user smiles as broadly as possible. Two smiles separated by at least 10-15 sec are sufficient.

8. Return to Normal Breathing (NB). The user repeats exercise number one.

After the exercise set is completed, the operator should check the calibration of the instrumentation and note any drift from the 0 or 100% baselines.

The preferred method of analyzing the exercise test data is to use a strip-chart recorder/integrator. With such a device, the operator will have complete control over the starting and terminating point of each exercise. The integrator will calculate, in near-real time, a time-averaged area under the leakage curve for each exercise and display/record a numerical value. An arithmetic average of the exercise leak concentrations can then be calculated, as well as an arithmetic average of the beginning and final ambient challenge concentrations. With these two arithmetic averages, the protection factor for the respirator can readily be calculated as defined earlier in this report.

Appropriately documented test records, compatible with the organization's needs, should be kept.

REFERENCES

1. Adley, F. E., and R. J. Uhle. Prot[illegible]n factors of self-contained compressed-air breathing apparatus [illegible]nd Hyg Assoc J 30:355-359 (1969).

2. Adley, F. E., and D. E. Wisehar[illegible]. Methods for performance testing of respiratory protective equi[illegible]nt. Am Ind Hyg Assoc J 23:251-256 (1962).

3. Albro, P. W., and R. O. Thomas. Enzymatic hydrolysis of di(2-ethylhexyl) phthalate by lipases. Biochim Biophys Acta 360:380-390 (1973).

4. Albro, P. W., et al. Metabolism of diethylhexyl phthalate by rats--isolation and characterization of the urinary metabolites. J Chromatogr 76:321-330 (1973).

5. Altschuler, B., et al. Aerosol deposition in the human respiratory tract. AMA Arch Ind Health 15:293-303 (1957).

6. Amberg, S., and F. Helmholz. The fatal dose of various substances on intravenous injection in the guinea pig. J Pharmacol Exp Ther 6:595 (1914).

7. Analytical integrating recorders, Sales Catalog, pp. 5-14. Horizon Ecology Company, 7435 North Oak Park Avenue, Chicago IL 60648, Telephone: (312) 647-7644, Jul 1979.

8. Autian, J. Toxicity and health threats of phthalate esters: Review of the literature. Environ Health Perspect 4:3-26 (1973).

9. Autian, J. Toxicity, untoward reactions, and related considerations in the medical use of plastics. J Pharm Sci 53:1289-1301 (1964).

10. Baker, R. W. R. Diethylhexyl phthalate as a factor in blood transfusion and haemodialysis. Toxicology 9:319-329 (1978).

11. Bales, R. E. Fluorocarbons--an industrial hygiene survey of worker exposure in four facilities. Dept of HEW, NIOSH, Cincinnati OH, NIOSH 79-101, Oct 1978.

12. Balieu, E. Characterization of respirator adsorbent filters by means of penetration curve parameters. Ann Occup Hyg 19:203-213 (1976).

13. Barraclough, R. N. Modern concepts of respiratory protection. Ann Occup Hyg 19:351-355 (1976).

14. Barton, D. Aerosolized detergents and mucolytic agents in the treatment of stable chronic obstructive pulmonary disease. Am Rev Respir Dis 110:104-110 (1974).

15. Billups, N. B., and F. W. Oberst. Chloropicrin leakage test of the M17 protective mask equipped with drinking and resuscitation devices worn by volunteers. U.S. Army Edgewood Arsenal, CRDL Technical Memorandum 2-32, Oct 1965.

16. Bolton, N. E. Oak Ridge National Laboratory Respirator Program--a programmatic description. AEC Contract W-7405-ENG-26, ORNL-TM-4719, Oct 1974.

17. Bornmann, G., et al. Uber das Verhalten des Organismus bei Einwirkung verschiedener Weichmacher. Z Lebensm Unters Forsch 13:413-424 (1956).

18. Bower, R. K., et al. Teratogenic effects in the chick embryo caused by esters of phthalic acid. J Pharmacol Exp Ther 171:314-324 (1970).

19. Boyd, E. M. 100-day LD_{50} index of chronic toxicity. Clin Toxicol 4:205-213 (1971).

20. Boyd, E. M., et al. The chronic oral toxicity of sodium chloride at the range of the LD_{50}(0.1 L). Can J Physiol Pharmacol 44:157-172 (1966).

21. Boyd, E. M., and M. N. Shanas. The acute oral toxicity of sodium chloride. Arch Int Pharmacodyna Ther 144:86-96 (1963).

22. Braun, B., et al. Die Verwendung von Kunststoffen als Verpackungsmaterial in der Medizinisch-Pharmazeutsche Praxis. Dtsch Apotheker Zeitung 33:1011-1015 (1961).

23. Brevik, E. M. Toxicity of the PVC-plasticizer di(2-ethylhexyl) phthalate. Nord Vet 28:226-232 (1976).

24. Brown, V. K., et al. A contribution to the toxicology of some alcohol mixtures containing 7 to 9 and 9 to 11 carbon atoms and the corresponding phthalate esters. Arch Toxicol 26:84-90 (1970).

25. Burgess, W. A., and W. C. Hinds. Performance and acceptance of respiratory facial seals. Ergonomics 13:455-464 (1970).

26. Burgess, W. A., and C. R. Parker. Supply rates for powered air-purifying respirators. Am Ind Hyg Assoc J 30:1-6 (1969).

27. Burgess, W. A., et al. A new technique for evaluating respirator performance. Am Ind Hyg Assoc J 22:422-429 (1961)

28. Calley, D., et al. Toxicology of a series of phthalate esters. J Pharm Sci 55:158-162 (1966).

29. Calvin, M. E., et al. Hazards to health--salt poisoning. N Engl J Med 270:625-626 (1964).

30. Campbell, H. L. Sodium chloride as an adjunct to a diet of whole wheat and whole milk. Am J Physiol 147:340-342 (1946).

31. Carpenter, C. P., et al. Chronic oral toxicity of di(2-ethylhexyl) phthalate for rats, guinea pigs, and dogs. AMA Arch Ind Hyg Occup Med 8:219-226 (1953).

32. Carter, R. F., and B. J. Fotheringham. Fatal salt poisoning due to gastric lavage with hypertonic saline. Med J Aust 1:539-541 (1971).

33. Catalog and buyers guide, Pollution Equipment News, Vol. 11, No. 6, p. 324, Integrating Strip Chart Recorders Advertisement, Linear Instruments, 17282 Eastman Ave, Irvine CA 92714, Telephone: (714) 546-6776, 1979.

34. Chromatography Catalog No. 19, pp. 98-101. Varian Instrument Group, Customer Service Center, 220 Humboldt Court, Sunnyvale CA 94086, Telephone: (408) 734-5370, 1979.

35. Corn, M., et al. Response of cats to inhaled mixtures of SO_2 and SO_2-NaCl aerosol in air. Arch Environ Health 24:248-256 (1972).

36. Cyr, R. R., and D. W. Watkins. Facepiece-to-face leakage evaluation using a helium leak detection method. J Vacuum Sci Technol 12:419-422 (1975).

37. Dahl, L. K. Effects of chronic excess salt feeding--elevation of plasma cholesterol in rats and dogs. J Exper Med 112:635-651 (1960).

38. Dahl, L. K., and R. A. Love. Evidence for a relationship between sodium chloride intake and human essential hypertension. AMA Arch Int Med 94:525-531 (1954).

39. Dangers, R. President, National Draeger Incorporated, Parkway View Drive, Pittsburgh, Pennsylvania 15205, Tele: (412) 787-1131. Technical Brochure for: Model 80 Face Mask Fit-Tester; Draeger Review, Vol. 41, Jun 1978, and Draeger Review, Vol. 42, Dec 1978.

40. Daniel, J. W. Toxicity and metabolism of phthalate esters. Clin Toxicol 13:257-268 (1978).

41. Daniel, J. W., and H. Bratt. The absorption, metabolism and tissue distribution of di(2-ethylhexyl) phthalate in rats. Toxicology 2:51-65 (1974).

42. Dautrebande, L. Microaerosols, New York: Academic Press, 1962.

43. Dautrebande, L., et al. Lung deposition of fine dust particles. AMA Arch Ind Health 16:179-187 (1957).

44. Dautrebande, L., et al. Studies on deposition of submicronic dust particles in the respiratory tract. AMA Arch Ind Health 19:383-391 (1959).

45. Dautrebande, L., and W. Walkenhorst. Deposition of NaCl microaerosols in the respiratory tract. Arch Environ Health 3:411-419 (1961).

46. Davis, T. O., et al. Respirator studies for the DOE Division of Operational and Environmental Safety. Progress Report: October 1, 1976 through September 30, 1977, Los Alamos Scientific Laboratory, LA-6969-PR, Apr 1978.

47. De Haan, R. L. Toxicity of tissue culture media exposed to polyvinyl chloride plastic. Nature--New Biology 231:85-86 (1971).

48. De Steiguer, D., et al. The use of n-pentane as a tracer gas for the quantitative evaluation of aircrew protective breathing equipment. Proceedings of the Fourteenth Annual SAFE Symposium, pp. 15-19, Sep 1976.

49. De Steiguer, D., et al. The objective evaluation of aircrew protective breathing equipment: II. Fullface masks and hoods. Proceedings of the Fourteenth Annual SAFE Symposium, pp. 10-12, Sep 1976.

50. Dillingham, E. O., and J. Autian. Teratogenicity, mutagenicity, and cellular toxicity of phthalate esters. Environ Health Perspect 4:81-89 (1973).

51. Documentation of the threshold limit values for substances in workroom air, Third Edition, American Conference of Governmental Industrial Hygienists, 1978.

52. Dorman, R. G., et al. A comparison of faceseal leakages measured by the argon and sodium flame tests. Test Report, UK Chemical Establishment, Porton Down, United Kingdom, October 15, 1970.

53. Douglas, D. D., et al. Respirator studies for the National Institute for Occupational Safety and Health. Progress Report: July 1, 1974 through June 30, 1975, Los Alamos Scientific Laboratory, LA-6386-PR, Aug 1976.

54. Drinker, P., et al. Quantitative measurements of the inhalation, retention, and exhalation of dusts and fumes by man: I. Concentrations of 50 to 450 mg per-cubic-meter. J Ind Hyg 10:13-24 (1928).

55. Eckardt, R. E., and R. Hindin. The health hazards of plastics. J Occup Med 15:308-319 (1973).

56. Ettinger, H. J., et al. Aerosol research and development related to health hazard analysis. Progress Report: July 1 through December 31, 1973, Los Alamos Scientific Laboratory, LA-5555-PR, Apr 1974.

57. Ettinger, H. J., et al. Aerosol research and development related to health hazard analysis. Progress Report: January 1 through June 30, 1973, Los Alamos Scientific Laboratory, LA-5359-PR, Jul 1973.

58. Federal Register, Volume 37, Number 59, Part II, Title 30, Respiratory protective devices; tests for permissibility; fees, pp. 6244-6271, Mar 25, 1972.

59. Ferber, B. I. Bureau of Mines respirator approval schedules: New and revised. Am Ind Hyg Assoc J 27:110-114 (1966).

60. Ferber, B. I., et al. Penetration of sodium chloride aerosol through respirator filters. Am Ind Hyg Assoc J 33:791-796 (1972).

61. Ferber, B. I., et al. Respiratory filter penetration using sodium chloride aerosol. Bureau of Mines report of investigations: 7403, Jun 1970.

62. Fevrier, D. Heimbehandlung dei Chronischen Ateminsuffizienz: Tragerlosungen fur Aerosolinhalationen. Schweiz Med Wochenschr 105:903-904 (1975).

63. First Draft STANAG (Standard NATO Agreement) No. 3864 AMD - The measurement of protection provided to the respiratory tract and eyes against NBC agents in particulate, aerosol, and vapour form. North Atlantic Treaty Organization, 29 Mar 1979.

64. Garvin, P. J., et al. A teratologic evaluation of plasma-soluble extracts of polyvinyl chloride plastics. Pharmacologist 18:231 (1976).

65. Gesler, R. M. Toxicology of di-2-ethylhexyl phthalate and other phthalic acid ester plasticizers. Environ Health Perspect 4:73-79 (1973).

66. Gibson, T. P., et al. Delivery of di-2-ethylhexyl phthalate to patients during hemodialysis. J Lab Clin Med 87:519-524 (1976).

67. Gleason, M. N., et al. Clinical toxicology of commercial products, Fourth Edition, Baltimore: The Williams and Wilkins Company, 1976.

68. GM bars dioctyl phthalate. Chemical and Engineering News, p. 7, Mar 27, 1972.

69. Goodman, L. S., and A. Gilman. The pharmacological basis of therapeutics, Fourth Edition. New York: Macmillan, 1975.

70. Graham, P. R. Phthalate ester plasticizer--why and how they are used. Environ Health Perspect 4:3-12 (1973).

71. Grant, H., and F. Reischsman. The effects of the ingestion of large amounts of sodium chloride on the arterial and venous pressures of normal subjects. Am Heart J 32:704-712 (1946).

72. Griffin, O. G., and P. J. Longson. The hazard due to inward leakage of gain to a full face mask. Ann Occup Hyg 13:147-151 (1970).

73. Grollman, A., et al. Sodium restriction in the diet for hypertension. JAMA 129:533-537 (1945).

74. Grollman, A., et al. Therapeutics of experimental hypertension. J Pharmacol Exp Ther 69:76-9 (1940).

75. Gross, F. Die Wirkung Von Desoxycorticosteronacetat Und Kochsalz Auf Den Experimentellen Hochdruck Der Ratte. Arch Int De Pharmacodyn Ther 131:211-221 (1950).

76. Guess, W. L. Toxicity profiles of vinyl and polyolefinic plastics and their additives. J Biomed Mater Res 2:313-335 (1968).

77. Guess, W. L., et al. Characterization of subtle toxicity of certain plastic components used in manufacture of the polyvinyls. Am J Hosp Pharm 24:495-501 (1967).

78. Guess, W. L., et al. A study of polyvinyl chloride--blood bag assemblies: Alteration or contamination of ACD solutions. Drug Intelligence 1:120-127 (1967).

79. Guyton, H. G., et al. Evaluation of respiratory protection of contagion masks. Appl Microbiol 4:141-143 (1956).

80. Guyton, H. G., and H. M. Decker. Respiratory protection provided by five new contagion masks. Appl Microbiol 11:66-68 (1963).

81. Guyton, H. G., and F. T. Lense. Methods for evaluating respiratory protective masks and their component parts. Arch Ind Health 14:246-249 (1956).

82. Guyton, H. G., et al. Techniques for evaluating biological penetration of respiratory masks on human subjects. Am Ind Hyg Assoc J 28:462-467 (1967).

83. Guyton, H. G., et al. Techniques for evaluating biological penetration of respiratory masks on humans. Dept of the Army, Fort Detrick, Frederick, Maryland, Technical Manuscript 380, NTIS AD817120, Jun 1967.

84. Hack, A., et al. Selection of respirator test panels representative of U.S. adult facial sizes. Los Alamos Scientific Laboratory, LA-5488, Mar 1974.

85. Harris, D. K. Health problems in the manufacture and use of plastics. Br J Ind Med 10:225-268 (1953).

86. Harris, D. K. Some hazards in the manufacture and use of plastics. Br J Ind Med 16:221-229 (1959).

87. Harris, R. S., et al. Chronic oral toxicity of 2-ethylhexyl phthalate in rats and dogs. AMA Arch Ind Hyg and Occup Med 13:259-264 (1956).

88. Hawley, G. G. The condensed chemical dictionary, Ninth Edition. New York: Van Nostrand Reinhold Company, 1977.

89. Hayashi, S., et al. Phthalate esters of Cryptotaenia Canadensis D.C. Var. Japonica Makino (Umbelliferae). Tetrahedron Letters 50:5061-5063 (1967).

90. Hayes, J. A., et al. The evaluation of biochemical damage in the rat lung after acute cadmium exposure. Am Rev Respir Dis 113:121-130 (1976).

91. Held, B. J., et al. Evaluation of one-year results of the full-face respirator quantitative man-test fitting program at the Lawrence Livermore Laboratory. AEC Contract W-7405-ENG-48, NTIS UCRL-52187, December 8, 1976.

92. Held, B. J., et al. Respirator studies for the National Institute for Occupational Safety and Health. Progress Report: July 1, 1973 through June 30, 1974, LA-5805-PR, Dec 1974.

93. Hillman, L. S., et al. Identification and measurement of plasticizer in neonatal tissues after umbilical catheters and blood products. N Engl J Med 292:381-386 (1975).

94. Hodge, H. C. Acute toxicity for rats and mice of 2-ethyl hexanol and 2-ethyl hexyl phthalate. Proc Soc Exp Biol Med 53:20-23 (1943).

95. Hodge, H. C., et al. Acute toxicity for mice of phthalic acid and certain derivatives. Proc Soc Exp Biol Med 49:471-473 (1942).

96. Homrowski, S., and M. Nikonorow. Toksycznosc Ostra Ftalanu Dwubutylu Oraz Ftalanu Dwn-2-Cty Loheksylu Produkcji Krajowej. Rocz Panstw Zakl Hig 10:321-327 (1959).

97. Hounam, R. F., et al. The evaluation of protection provided by respirators. Ann Occup Hyg 7:353-363 (1964).

98. Hyatt, E. C. Current problems in the field of respiratory protection. Am Ind Hyg Assoc J 19:121-122 (1958).

99. Hyatt, E. C. Respirator protection factors. Los Alamos Scientific Laboratory, LA-6084-MS, Jan 1976.

100. Hyatt, E. C., et al. Respirator studies for the AEC Division of Operational Safety. Los Alamos Scientific Laboratory, Progress Report: January 1 through June 30, 1973, LA-5470-PR, Dec 1973.

101. Hyatt, E. C., et al. Respiratory studies for the National Institute for Occupational Safety and Health. Progress Report: July 1, 1972 through June 3, 1973, Los Alamos Scientific Laboratory, LA-5620-PR, May 1974.

102. Hyatt, E. C., et al. Respirator efficiency measurement using quantitative DOP man tests. Am Ind Hyg Assoc J 33:635-643 (1972).

103. Hyatt, E. C., et al. Respirator research and development related to quality control. Los Alamos Scientific Laboratory, Quarterly Report: July 1 through September 30, 1971, LA-4908-PR, Mar 1972.

104. Hyatt, E. C., and C. P. Richards. A study of facepiece leakage of self-contained breathing apparatus by DOP man tests. Los Alamos Scientific Laboratory, Progress Report: July 1, 1971 through February 29, 1972, LA-4927-PR, Apr 1972.

105. Jacobson, M. S., et al. Physiologically solubilized di-2-ethylhexyl phthalate and its effect on the intact rhesus monkey. Toxicol Appl Pharmacol 33:168-169 (1975).

106. Jacobson, M. S., et al. The toxicity of human serum in flexible polyvinylchloride containers on human fibroblast cell cultures: An effect of di-2-ethylhexyl phthalate. Res Commun Chem Pathol Pharmacol 9:315-323 (1974).

107. Jaeger, R. J., and R. J. Rubin. di-2-ethylhexyl phthalate - A plasticizer contaminant of platelet concentrates. Transfusion 13:107-108 (1973).

108. Jaeger, R. J., and R. J. Rubin. Extraction, localization, and metabolism of di-2-ethylhexyl phthalate from PVC plastic medical devices. Environ Health Perspect 4:95-102 (1973).

109. Jaeger, R. J., and R. J. Rubin. Migration of a phthalate ester plasticizer from polyvinyl chloride blood bags into stored human blood and its localization in human tissues. N Engl J Med 287:1114-1118 (1972).

110. Jaeger, R. J., and R. J. Rubin. Phthalate ester metabolism in the isolated perfused rat liver system. Environ Health Perspect 4:49-51 (1973).

111. Jaeger, R. J., and R. J. Rubin. Plasticizers from plastic devices: Extraction, metabolism, and accumulation by biological systems. Science 170:460-462 (1970).

112. Jones, A. E., et al. Phthalate ester toxicity in human cell cultures. Toxicol Appl Pharmacol 31:283-289 (1975).

113. Juvalta, N. Ist der Benzolkern in Thierkorper Zerstorbar? Z Physiologische Chemie 14:26-31 (1889).

114. Karel, L., et al. The intraperitoneal toxicity of some glycols, glycol ethers, glycol esters, and phthalates in mice. J Pharmacol Exp Ther 90:338-347 (1947).

115. Kelly, J. F., et al. Acute airway obstruction in rhesus monkeys induced by pharmacologic and immunologic stimuli. J Lab Clin Med 83:738-749 (1974).

116. Kim, S. W., et al. Effect of phthalate plasticizer on blood compatability of polyvinyl chloride. J Pharm Sci 65:670-673 (1976).

117. Klaassen, C. D. Comparison of the toxicity of chemicals in newborn rats to bile duct-ligated and sham operated rats and mice. Toxicol Appl Pharmacol 24:37-44 (1973).

118. Klimmer, O. R., and I. U. Nebel. Experimentelle Untersuchungen Zur Frage der Toxizitat einiger Stabilisatoren in Kunststoffen aus Polyvinyl-chlorid. Arzneim-Forsch 10:44-48 (1960).

119. Koletsky, S. Role of salt and renal mass in experimental hypertension. AMA Arch Pathol 68:21-32 (1959).

120. Krakower, C. A., and M. Goettsch. Effect of excessive ingestion of sodium chloride on the chick with particular reference to renal changes. Arch Pathol 40:209-219 (1945).

121. Krakower, C. A., and H. E. Heino. Relationship of growth and nutrition to cardiorenal changes induced in birds by a high salt intake. Arch Pathol 44:143-162 (1947).

122. Krauskopf, L. G. Studies on the toxicity of phthalates via ingestion. Environ Health Perspect 4:61-72 (1973).

123. Ladd, M., and L. G. Raisz. Response of the normal dog to dietary sodium chloride. Am J Physiol 159:149-152 (1949).

124. Lake, B. G., et al. Studies on the effects of orally administered di(2-ethylhexyl) phthalate in the ferret. Toxicology 6:341-356 (1976).

125. Lake, B. G., et al. Studies on the hepatic effects of orally administered di(2-ethylhexyl) phthalate in the rat. Toxicol Appl Pharmacol 32:355-367 (1975).

126. Lake, B. B., et al. Studies on the effects of the oral administration of di(2-ethylhexyl) phthalate on some hepatic enzymes in the rat. Biochem Soc Trans 2:322-325 (1974).

127. Landahl, H. D. On the removal of air-borne droplets by the human respiratory tract: I. The lung. Bull Math Biophys 12:43-56 (1950).

128. Landahl, H. D., et al. On the retention of air-borne particulates in the human lung: II. Arch Ind Hyg Occup Med 3:359-366 (1951).

129. Landahl, H. D., et al. Retention of air-borne particulates in the human lung: III. Arch Ind Hyg Occup Med 6:508-577 (1952).

130. Laurain, A. R. Acute fatal bronchitis and pneumonia associated with exposure to Freon-12. Ind Med Surg 33:469 (1964).

131. Lawrence, W. H., et al. A toxicological investigation of some acute, short-term, and chronic effects of administering di-2-ethylhexyl phthalate (DEHP) and other phthalate esters. Environ Res 9:1-11 (1975).

132. Lawrence, W. H., et al. Toxicity of plastics used in medical practice I: Investigation of tissue response in animals by certain unit packaged polyvinyl chloride administration devices. J Pharm Sci 52:958-963 (1963).

133. Lawson, J. J. The toxicity of titanium tetrachloride. J Occup Med 3:7-12 (1961).

134. Lee, H. Y., et al. Toxicity of di(2-ethylhexyl) phthalate in chick embryos: Gel electrophoretic analysis of serum proteins. Comp Biochem Physiol 56:9-12 (1977).

135. Lee, H. Y., and G. W. Kalmus. Cytotoxic effect of di-2-ethylhexyl phthalate on cultured chick embryonic cells. Experientia 30:800-801 (1974).

136. Lee, H. Y., et al. Effects of phthalate esters (plasticizers) on chick embryos and chick embryonic cells. Growth 38:301-302 (1974).

137. Lefaux, R. Practical toxicology of plastics. CRC Press, International Scientific Series, 1968.

138. Lehman, A. J. Insect repellents. Association of Food and Drug Officials Quarterly Bulletin, pp. 87-89, Jul 1954.

139. Leigh, J. D. Quantitative respirator man-testing and anthropometric survey. AEC Contract AT(29-1)-1106, May 22, 1975, NTIS RFP 2358, TID-4500-R62.

140. Leigh, J. D. Quantitative respirator man-testing at Rocky Flats. Rockwell International, Atomics International Division, Rocky Flats Plant, Golden, Colorado, RFP-2433.

141. Lenel, R., et al. Arterial hypertension in the chicken. Am J Physiol 152:557-562 (1948).

142. Lester, D., and L. A. Greenberg. Acute and chronic toxicity of some halogenated derivatives of methane and ethane. Arch Ind Hyg Occup Med 2:335-344 (1950).

143. Lester, D., and L. A. Greenberg. The toxicity of sulfur hexafluoride. Arch Ind Hyg Occup Med 2:348-349 (1950).

144. Lewis, R. C., et al. The effect of excessive dietary sodium and potassium on the carbohydrate metabolism of normal rats. J Nutr 27:11-21 (1944).

145. Lilienfeld, P., et al. Development of a prototype fibrous aerosol monitor. Am Ind Hyg Assoc J 40:270-282 (1979).

146. Loke, J., et al. The effect of intermittent positive pressure breathing on maximum expiratory flow-volume curves with air and helium-oxygen. Clin Res 23:350 (1975).

147. Lowry, P. L., et al. Respirator studies for the National Institute for Occupational Safety and Health. Progress Report: July 1, 1975 through December 31, 1976, Los Alamos Scientific Laboratory, LA-6722-PR, Feb 1977.

148. Lowry, P. L., et al. Performance of single-use respirators. Am Ind Hyg Assoc J 38:462-467 (1977).

149. Lowry, P. L., et al. Respirator studies for the National Institute for Occupational Safety and Health. Progress Report: January 1 through December 31, 1977, Los Alamos Scientific Laboratory, LA-7317-PR, Jun 1978.

150. Lowry, P. L., et al. Quantitative fit-test method for powered air-purifying respirators. Am Ind Hyg Assoc J 40:291-299 (1979).

151. Luxon, S. G. Harmonization of respirator standards in Europe. Am Ind Hyg Assoc J 34:143-149 (1973).

152. Luxon, S. G. The use of dust respirators against asbestos dust hazards in the United Kingdom. Am Ind Hyg Assoc J 32:723-725 (1971).

153. Main, R. J. Mineral salts as toxic factors in urinary prolan concentrates. Endocrinology 24:523-525 (1939).

154. Malette, F. S., and E. Von Haam. Studies on the toxicity and skin effects of compounds used in the rubber and plastics industries: II. Plasticizers. AMA Arch Ind Hyg Occup Med 6:231-236 (1952).

155. Malik, S. K. Decrease in specific airway conductance following inhalation of nebulized aerosols. Indian J Chest Dis 15:272-275 (1973).

156. Marcel, Y. L. Determination of di-2-ethylhexyl phthalate levels in human blood plasma and cryoprecipitates. Environ Health Perspect 4:119-121 (1973).

157. Marcel, Y. L., and S. P. Noel. A plasticizer in lipid extracts of human blood. Chem Phys Lipids 4:418-419 (1974).

158. Marcel, Y. L., and S. P. Noel. Contamination of blood stored in plastic packs. Lancet 1:35-36 (1970).

159. Mathur, S. P. Respirometric evidence of the utilization of di-octyl and di-2-ethylhexyl phthalate plasticizers. J Environ Quality 3:207-209 (1974).

160. Mayer, F. L., and H. O. Sanders. Toxicology of phthalic acid esters in aquatic organisms. Environ Health Perspect 4:153-157 (1973).

161. McConville, J. T. Human variability and respirator sizing. Dept of HEW, NIOSH, Cincinnati OH, NIOSH 76-146, Mar 1976.

162. McGinnis, N. J. Exhalation valve leakage test. Dept of HEW, Appalachian Laboratory for Occupational Safety and Health, Testing and Certification Branch, Morgantown WV, NIOSH/TC/R-005, NTIS PB-252692, Feb 1976.

163. McJilton, C. E., et al. Influence of relative humidity on functional effects of an inhaled SO_2 - Aerosol mixture. Am Rev Respir Dis 113: 163-169 (1976).

164. McLaughlin, J., et al. The injection of chemicals into the yolk sac of fertile eggs prior to incubation as a toxicity test. Toxicol Appl Pharmacol 5:760-771 (1963).

165. Meneely, G. R., et al. Renal damage in rats fed large quantities of sodium chloride. J Clin Invest 31:650 (1952).

166. Meneely, G. R., et al. Chronic sodium chloride toxicity in the albino rat. J Nutr 48:489-498 (1952).

167. Meneely, G. R., et al. Chronic sodium chloride toxicity in the albino rat--Occurrence of hypertension and of a syndrome of edema and renal failure. J Exp Med 98:71-83 (1953).

168. Mes, J., et al. Dibutyl and di-2-ethylhexyl phthalate in human adipose tissue. Bull Environ Contam Toxicol 12:721-725 (1974).

169. Metcalf, R. L., et al. Uptake and fate of di-2-ethylhexyl phthalate in aquatic organisms and in a model ecosystem. Environ Health Perspect 4:27-34 (1973).

170. Method for sodium chloride particulate test for respirator filters. British Standards Institution, BS 4400:1969.

171. Meyer, J. H., et al. Effect of dietary levels of sodium chloride and potassium on growth and on concentrations in blood plasma and tissues of the white rat. Am J Physiol 162:182-188 (1950).

172. Milburn, R. H., et al. The retention of hygroscopic dusts in the human lungs. AMA Arch Ind Health 1:59-62 (1957).

173. Miller, W. C., and R. Awe. Effect of nebulized lidocaine on reactive airways. Am Rev Respir Dis 111:739-741 (1975).

174. Minutes of the ASTM E-34.14 Task Group--Respirators. February 17-18, 1979, pp. 1-72.

175. Minutes of the Respiratory Quantitative Fit Testing Standards Workshop, Los Alamos Scientific Laboratory, March 8-9, 1977, pp. 1-59.

176. Mitchell, R. N., et al. Comparison of respirator filter penetration by dioctyle phthalate and sodium chloride. Am Ind Hyg Assoc J 32:357-364 (1971).

177. Morrow, P. E., et al. An experimental study of aerosol deposition in human subjects. AMA Arch of Ind Health 18:292-298 (1958).

178. Munch, J. C. Aliphatic alcohols and alkyl esters: Narcotic and lethal potencies to tadpoles and to rabbits. Ind Med 41:31-33 (1972).

179. Munsen, L. G. Double-bibbed supplied-air hood. EG & G Idaho Inc., Dept of Energy Contract EY-76-C-07-1570. TREE-1214, NTIS TID-4500, R66, Feb 1978.

180. Myers, G. E. Effect of sampling lines on measured DOP aerosol concentration. Am Ind Hyg Assoc J 35:307-310 (1974).

181. Myers, W. R. Silica dust test for respiratory protective devices. Dept of HEW, Appalachian Laboratory for Occupational Safety and Health, Testing and Certification Branch, Morgantown WV, NIOSH/TC/R-007, NTIS PB-278019, Jul 1977.

182. Nazir, D. J., et al. Isolation, identification, and specific localization of di-2-ethylhexyl phthalate in bovine heart muscle mitochondria. Biochemistry 10:4228-4232 (1971).

183. Neergaard, J., et al. On the exudation of plasticizers from PVC haemodialysis tubings. Nephron 14:263-274 (1975).

184. Nelson, G. O., and C. A. Harder. Hazards Control Progress Report No. 45, January through April 1973: Calculation of Respirator Cartridge Service. AEC Contract W-7405-ENG-48, NTIS UCRL-50007-73-1, Jun 1, 1973.

185. Nelson, G. O., and C. A. Harder. Respirator cartridge efficiency studies: IV. Effects of steady-state and pulsating flow. Am Ind Hyg Assoc J 33:797-805 (1972).

186. Nelson, G. O., and C. A. Harder. Respiratory cartridge efficiency studies: V. Effect of solvent vapor. Am Ind Hyg Assoc J 34:391-410 (1974).

187. Nelson, G. O., and D. J. Hodgkins. Respirator cartridge efficiency studies: II. Preparation of test atmospheres. Am Ind Hyg Assoc J 33:110-116 (1972).

188. Nematollahi, J., et al. Plasticizers in medical application. I. Analysis and toxicity evaluation of dialkyl benzene-dicarboxylates. J Pharm Sci 56:1446-1453 (1967).

189. Nikonorow, M., et al. Effect of orally administered plasticizers and polyvinyl chloride stabilizers in the rat. Toxicol Appl Pharmacol 26:253-259 (1973).

190. NIOSH's Appalachian Center for Occupational Safety and Health, Morgantown WV, National Safety News, pp. 96-101, Sep 1974.

191. Nishimura, H., and S. Miyamoto. Teratogenic effects of sodium chloride in mice. Acta Anatomica 74:121-124 (1969).

192. Oba, T., et al. Safety of phthalic acid esters--especially DEHP. Eisei Shikenjo Hokoku (Bulletin of the National Institute of Hygienic Sciences), Tokyo 93:1-25 (1975).

193. Occupational diseases--A guide to their recognition, Revised Edition, U.S. Department of Health, Education, and Welfare, National Institute for Occupational Safety and Health, NIOSH Publication No. 77-181, Jun 1977.

194. Oettel, H. Gesundheitsgefahrdung durch Kunstsoffe? Naunyn Schmiedebergs Arch Exp Pathol Pharmakol 232:77-137 (1957-1958).

195. Ogner, G., and M. Schnitzer. Humic substances: Fulvic acid--dialkyl phthalate complexes and their role in pollution. Science 170:317-318 (1970).

196. Ohyama, T. Effects of phthalate esters on glucose 6-phosphate dehydrogenase and other enzymes in vitro. Toxicol Appl Pharmacol 40:355-364 (1977).

197. Packard, L. H., et al. Quantitative fit testing of personnel utilizing a mouthpiece respirator. Am Ind Hyg Assoc J 39:723-730 (1978).

198. Paez, P. N., and W. F. Miller. Surface active agents in sputum evacuation: A blind comparison with normal saline solution and distilled water. Chest 60:312-317 (1971).

199. Palmer, K. C., et al. Cellular proliferation induced in the lung by cadmium aerosol. Am Rev Respir Dis 112:173-179 (1975).

200. Parmeggiani, L., and C. Sassi. Rischi E Patologia Professionale Nella Produzione E Nella Lavorazione Di Alcune Materie Plastiche. Med Lav 46:14-24 (1955).

201. Patty, F. A. Industrial hygiene and toxicology. Second Edition. New York: John Wiley & Sons, 1963.

202. Paulet, G., et al. Toxicite chronique a moyen terme de deux hydrocarbures chlorofluores: R_{11} et R_{12}. Arch Mal Prof Med Travail Securite Sociale 28:464-469 (1967).

203. Pavia, D., et al. Enhanced clearance of secretions from the human lung after the administration of hypertonic saline aerosol. Am Rev Respir Dis 117:199-203 (1978).

204. Peakall, D. B. Effects of di-n-butyl and di-2-ethylhexyl phthalate on the eggs of ring doves. Bull Environ Contam Toxicol 12:698-702 (1974).

205. Peakall, D. B. Phthalate esters: Occurrence and biological effects. Residue Rev 54:1-41 (1975).

206. Perera, G. A., et al. Effect of desoxycorticosterone acetate on the blood pressure of man. J Am Med Assoc 125:1030-1035 (1944).

207. Peters, J. W., and R. M. Cook. Effect of phthalate esters on reproduction in rats. Environ Health Perspect 4:91-94 (1973).

208. Phthalate effect on health still not clear. Chem Eng News, pp. 14-15, Sep 8, 1972.

209. Piechocki, J. T., and W. C. Purdy. Determination of di(2-ethylhexyl) phthalate (DEHP) in human plasma. Clin Chim Acta 48:385-391 (1973).

210. Plasticizers fog windows. Chem Eng News, p. 17, Dec 13, 1971.

211. Plasticizers: Getting into blood. Chem Eng News, pp. 12-13, Feb 15, 1971.

212. Plasticizers: Pollution suspect. Chem Eng News, p. 8, Nov 1, 1971.

213. Pribram, E. Zur Lehre von den Physiologischen Wirkungen Carbocyclischer Sauren. Arch Exp-Pathol Pharmakol 51:372-382 (1904).

214. Pritchard, J. A. A guide to industrial respiratory protection. Dept. of HEW, NIOSH, Cincinnati, Ohio, NIOSH 76-189, Jun 1976.

215. Project: No. T-3, Test of expendable dust respirator: E5, Dept of the Army, Armored Medical Research Laboratory, Fort Knox, Kentucky, SPMEA 470.72, NTIS AD 655571, Aug 1967.

216. Registry of toxic effects of chemical substances, Vol. I and II, U.S. Department of Health, Education, and Welfare, National Institute for Occupational Safety and Health, 1977 Edition.

217. Respirator fit test. Ind Hyg News, Vol. 2, No. 3, p. 26, Jul 1979.

218. Responses of the rat adrenal to a high salt diet. Bull Johns Hopkins Hosp 139:44-45 (1951).

219. Revoir, W. H. Activities of the AIHA-ACGIH Respirator Committee during the past three years. Am Ind Hyg Assoc J 31:221-224 (1970).

220. Revoir, W. H. Comparison of performance characteristics of dust respirators made in the United States and the United Kingdom. Am Ind Hyg Assoc J 32:718-722 (1971).

221. Robinson, E., et al. A meteorological tracer technique using uranine dye. J Meteorology 16:63-67 (1959).

222. Roll, D. B., et al. GLC analysis of bis(2-ethylhexyl) phthalate plasticizer in tissue and plasma. J Pharm Sci 63:1628-1629 (1974).

223. Rosenbluth, S. A., et al. Tissue culture method for screening toxicity of plastic materials to be used in medical practice. J Pharm Sci 54:156-159 (1965).

224. Rowland, I. R., et al. Hydrolysis of phthalate esters by the gastrointestinal contents of the rat. Food Cosmet Toxicol 15:17-21 (1977).

225. Rubin, R. J., and R. J. Jaeger. Some pharmacologic and toxicologic effects of di-2-ethylhexyl phthalate (DEHP) and other plasticizers. Environ Health Perspect 3:53-59 (1973).

226. Rubin, R. J., and P. P. Nair. Plasticizers in human tissues. N Engl J Med 288:915-916 (1973).

227. Rubin, R. J., and C. A. Schiffer. Fate in humans of the plasticizer di-2-ethylhexyl phthalate arising from transfusion of platelets stored in vinyl plastic bags. Transfusion 16:330-335 (1976).

228. Ruch, W. E., et al. Respirator cartridge efficiency studies: I. Experimental design. Am Ind Hyg Assoc J 33:105-109 (1972).

229. Sackner, M. A., et al. Effects of nebulized ipratropium bromide and atropine sulfate on tracheal mucous velocity and lung mechanics in anesthetized dog. Respir 34:181-185 (1977).

230. Sackner, M. A., et al. Effects of sulfuric acid aerosol on cardiopulmonary function of dogs, sheep, and humans. Am Rev Respir Dis 118: 497-510 (1978).

231. Sackner, M. A., et al. Effect of sulfate aerosols on cardiopulmonary function of normal humans. Am Rev Respir Dis 115:240 (1977).

232. Sackner, M. A., et al. Effect of moderate duration exposures to sulfate and sulfuric acid aerosols on cardiopulmonary function of anesthetized dogs. Am Rev Respir Dis 117:257 (1978).

233. Sackner, M. A., and M. Reinhardt. Effect of microaerosols of sulfate particulate matter on tracheal mucous velocity in conscious sheep. Am Rev Respir Dis 115:241 (1977).

234. Sanders, H. O., et al. Toxicity, residue dynamics, and reproductive effects of phthalate esters in aquatic invertebrates. Environ Res 6:84-90 (1973).

235. Sapirstein, L. A., et al. Production of hypertension in the rat by substituting hypertonic sodium chloride solutions for drinking water. Proc Soc Exp Biol Med 73:82-85 (1950).

236. Sax, N. I. Dangerous properties of industrial materials. Second Edition. New York: Reinhold Publishing Corporation, 1963.

237. Sayers, G., et al. The effect of sodium chloride upon the disposition of injected glucose in a strain of rats. J Nutr 26:139-151 (1943).

238. Schmid, H., and P. Karrer. Uber Wasserlosliche Inhaltsstoffe von Papaver Somniferum. Helv Chim Acta 28:722-740 (1945).

239. Schmidt, J. G., et al. Effects of vehicle on the response to intravenous di(2-ethylhexyl) phthalate (DEHP) in rats. Toxicol Appl Pharmacol 33:169 (1975).

240. Schrager, K. J. Radon progeny inhalation study--final report, AEC Contract No. AT (11-1)-1500, June 1, 1965 - May 31, 1974.

241. Schulz, C. O., and R. J. Rubin. Distribution, metabolism, and excretion of di-2-ethylhexyl phthalate in the rat. Environ Health Perspect 4:123-129 (1973).

242. Schultz, C. O., et al. Acute lung toxicity and sudden death in rats following the intravenous administration of the plasticizer di(2-ethylhexyl) phthalate solubilized with tween surfactants. Toxicol Appl Pharmacol 33:514-525 (1975).

243. Seeman, J., et al. Di-2-Athylhexylphthalat in PVC-Ver-packten Plasmaersatzlosungen auf Dextranbasis-Bestimmung und Toxikologische Bewertung, Munchener Med Wochenschr 118:923-928 (1976).

244. Selye, H., et al. Influence of sodium chloride upon the actions of desoxycorticosterone acetate. Am Heart J 37:1009-1016 (1949).

245. Seth, P. K., et al. Effect of di-2-ethylhexyl phthalate (DEHP) on rat gonads. Environ Res 12:131-138 (1976).

246. Shaffer, C. B., et al. Acute and subacute toxicity of di(2-ethylhexyl) phthalate with note upon its metabolism. J Ind Hyg Toxicol 27:130-135 (1945).

247. Shibko, S. I., and H. Blumenthal. Toxicology of phthalic acid esters used in food-packaging material. Environ Health Perspect 4:131-137 (1973).

248. Singh, A. R., et al. Maternal-fetal transfer of ^{14}C-di-2-ethylhexyl phthalate and ^{14}C-diethyl phthalate in rats. J Pharm Sci 64:1347-1350 (1975).

249. Singh, A. R., et al. Mutagenic and antifertility sensitivities of mice to di-2-ethylhexyl phthalate (DEHP). Toxicol Appl Pharmacol 29:35-46 (1974).

250. Singh, A. R., et al. Teratogenicity of phthalate esters in rats. J Pharm Sci 61:51-55 (1972).

251. Skaats, C. D. Test development for full-face mask respiratory equipment. AEC Contract AT(29-1)-1106, May 22, 1975, NTIS RFP 1997.

252. Smith, S. B., and J. F. Strempfer. Determination of phthalate. Ind Eng Chem 16:416 (1944).

253. Smoot, D. M., and D. L. Smith. Development of improved respirator cartridge and cannister test methods. Prepared for NIOSH, Contract NAS 10-8842, NTIS PB-274756, Jul 1977.

254. Snook, S. H., et al. Respirator comfort: Subjective response to force applied to the face. Am Ind Hyg Assoc J 27:93-97 (1966).

255. Specification for respirators for protection against harmful dusts and gases. British Standards Institution, BS 2091:1969.

256. Srivastava, S. P., et al. Effect of di-2-ethylhexyl phthalate on the activity of succinic dehydrogenase and adenosine triphosphatase on some vital organs of the rat. Toxicology 7:163-168 (1977).

257. Srivastava, S. P., et al. Biochemical effects of di-2-ethylhexyl phthalate. Environ Physiol Biochem 5:178-183 (1975).

258. Stalling, D. L., et al. Phthalate ester residues--their metabolism and analysis in fish. Environ Health Perspect 4:27-34 (1973).

259. Stein, M. S., et al. Influence of dietary fat and di-2-ethylhexyl phthalate on tissue lipids in rats. J Nutr 104:187-191 (1974).

260. Stein, F., et al. The density of uranine aerosol particles. Am Ind Hyg Assoc J 27:428-430 (1966).

261. Steinberg, S. B. President, Air Techniques Incorporated, 1717 Whitehead Road. Baltimore, Maryland 21207, Tele: (301)944-6037. Technical brochure for: TDA-50 DOP Aerosol Man Test System, TDA-60 NaCl Aerosol Man Test System, TDA-80 DOP Portable Facefit Tester, and Price List effective 1 January 1979.

262. Stenchever, M. A., et al. Effects of bis(2-ethylhexyl) phthalate on chromosomes of human leukocytes and human fetal lung cells. J Pharm Sci 65:1648-1651 (1976).

263. Stern, I. J., et al. Physicochemical aspects of the extraction in blood and the disposition in rats of di(2-ethylhexyl) phthalate plasticizer. Toxicol Appl Pharmacol 41:507-522 (1977).

264. Suspected carcinogens--A subfile of the registry of toxic effects of chemical substances, U.S. Department of Health, Education and Welfare, National Institute for Occupational Safety and Health, Second Edition, 1976.

265. Swab, C. F., and B. I. Ferber. Freon 113 as a test material for chemical cartridge respirators. Bureau of Mines Report Investigations: 7380, May 1970.

266. Swinyard, E. A., et al. Nonspecific effect of bis(2-ethylhexyl) phthalate on hexobarbital sleep time. J Pharm Sci 65:733-734 (1976).

267. Takahashi, T. Biochemical studies on phthalic esters. II. Effects of phthalic esters on mitochondrial respiration of rat liver. Biochem Pharmacol 26:19-24 (1976).

268. Tankara, A., et al. Biochemical studies on phthalic esters. I. Elimination, distribution and metabolism of di(2-ethylhexyl) phthalate in rats. Toxicology 4:253-264 (1975).

269. Thames, F. C. Determination of phthalate plasticizers. Ind Eng Chem 3: 418-419 (1936).

270. Thiess, A. M., and I. Fleig. Chromosomenunter-suchungen bei Mitarbeitern mit Exposition gegenuber di-2-ethylhexylphthalat (DOP). Zentralbl Arbeitsmed Arbeitsschutz Prophyl 12:351-355 (1978).

271. Thiess, A. M., et al. Mortalitatsstudie bei Mitarbeitern mit Exposition gegenuber di-2-Ethylhexyl-phthalat (DOP). Jahrestagung Deutchen Gesellschraft Arbeitsmed 24:155-164 (1978).

272. Thiess, A. M., et al. Untersuchungen zur Morbidtat bei Mitarbeiternmit Exposition gegenuber di-2-Ethylhexylphthalat (DOP). Jahrestagung Deutchen Gesellschraft Arbeitsmed 24:137-154 (1978).

273. Thomas, G. H. Quantitative determination and confirmation of identity of trace amounts of dialkyl phthalates in environmental samples. Environ Health Perspect 4:23-28 (1973).

274. Thomas, J. A., et al. A Review of the biological effects of DI(2-ethylhexyl) phthalate. Toxicol Appl Pharmacol 45:1-27 (1978).

275. TLVs--Threshold limit values for chemical substances and physical agents in the workroom environment with intended changes for 1978. The American Conference of Governmental Industrial Hygienists, 1978.

276. Turner, J. H., et al. An evaluation of the effects of diethylhexyl phthalate (DEHP) on mitotically capable cells in blood packs. Transfusion 14:560-566 (1974).

277. U.S. Army Test and Evaluation Command Commodity Engineering Test Procedure: Breathing Apparatuses--Self-Contained Air/Oxygen Supply, Material Test Procedure 8-2-113, Deseret Test Center, NTIS AD868301, Jun 1969.

278. U.S. Army Test and Evaluation Command Commodity Engineering Test Procedure: Respirators, Material Test Procedure 8-2-114, Deseret Test Center, NTIS AD868303, May 1969.

279. Valeri, C. R., et al. Accumulation of di-2-ethylhexyl phthalate (DEHP) in whole blood, platelet concentrates, and platelet survival and function. Environ Health Perspect 4:103-118 (1973).

280. Verrett, M. J., et al. Teratogenic effects of captan and related compounds in the developing chicken embryo. Ann NY Acad Sci 160:334-343 (1969).

281. Waddell, W. J., et al. The distribution in mice of intravenously administered plasma solutions of [^{14}C] di-2-ethylhexyl phthalate determined by whole-body autoradiography. Toxicol Appl Pharmacol 39:339-353 (1977).

282. Wallin, R. F., et al. di(2-ethylhexyl) phthalate (DEHP) metabolism in animals and post-transfusion tissue levels in man. Bulletin of the Parenteral Drug Association 28:279-287 (1974).

283. Watson, H. A., et al. Evaluation of chemical cartridge respirator face fit. Bureau of Mines Report Investigations: 7431, Sep 1970.

284. White, J. M. Facepiece leakage and fitting of respirators. Paper presented at the First Canadian Conference on Protective Equipment, Toronto, Ontario, January 23-25, 1978, AECL-6175.

285. White, J. M. Respiratory fitting: The key to protecting workers. Occup Health Saf 47:22-25 (1978).

286. White, J. M., and R. J. Beal. The measurement of leakage of respirators. Am Ind Hyg Assoc J 27:239-242 (1966).

287. Wilhelmj, C. M., et al. Effect of prolonged high sodium chloride ingestion and withdrawal upon blood pressure of dogs. Proc Soc Exper Biol Med 77:379-382 (1951).

288. Williams, D. T., and B. J. Blanchfield. Retention, excretion and metabolism of di(2-ethylhexyl) phthalate administered orally to the rat. Bull Environ Contam Toxicol 11:371-378 (1974).

289. Williams, F. T. Notes on quantitative fit testing using Freon 12, sodium chloride, and DOP aerosol. Dynatech Frontier Corporation, June 30, 1977.

290. Williams, F. T. Some general properties of airborne particulates. Dynatech Frontier Corporation, Technical Note: TN 106.00, March 14, 1974.

291. Wilson, I. B., and V. K. LaMer. The retention of aerosol particles in the human respiratory tract as a function of particle radius. J Ind Hyg Toxicol 30:165-280 (1948).

292. Wilson, R. H., and W. E. McCormick. Toxicology of plastics and rubber. Ind Med Surg 13:479-486 (1954).

293. Wiswesser, W. J. Pesticide Index, Fifth Edition, The Entomological Society of America, Maryland, 1976.

294. Wright, C. L. President, Dynatech Frontier Corporation, P.O. Box 30041, Albuquerque, New Mexico 87110, Tele: (505) 266-7932. Technical brochure for: Model FE222 Test Booth; Model FE250A Portable DOP Aerosol Quantitative Man Fit Test System; Model FE257 Table-Top DOP Aerosol Quantitative Respirator Fit Test Instrument; Model FE259 Polydispersed DOP Aerosol Test System; Model FE560 Sodium Chloride Aerosol Test System; and Price List Effective May 1, 1979.

295. Wright, E. M. The Mound Laboratory Protection Program. Paper Presented at the Loss Prevention Conference, St. Louis, Missouri, Sep 27-30, 1976, MLM-2365 (OP).

296. Wylicil, P., and M. Beil. Wirksambeit und Organisation der Assistierenden Uberdruckbeatmung mit Aerosolinhal[illegible] bei Chronischen Obstruktiven Lungenkrankheiten. Dtsch Med Wochens[illegible] 99:1098-1103 (1974).

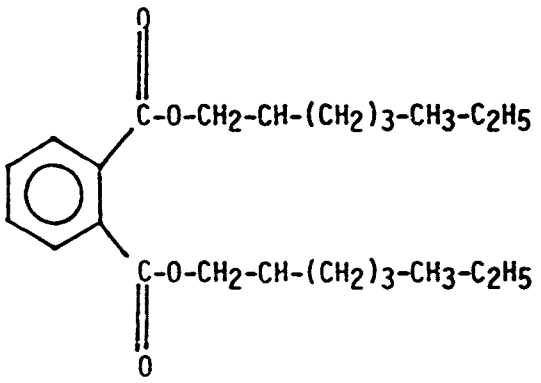
GLOSSARY

Aerosol. A colloidal system in which a gas, usually air, is the continuous medium, and particles of solid or liquid are dispersed in it.

Di-n-octyl Phthalate. Synonyms: Dioctyl Ester, Celluflex DOP, Dioctyl Phthalate, n-Dioctyl Phthalate, Octyl Phthalate, Polycizer 162, PX-138, O-Benzenedicarboxylic Acid, Dioctyl O-Benzenedicarboxylate

Molecular Formula: $C_6H_4[COOC_8H_{17}]_2$

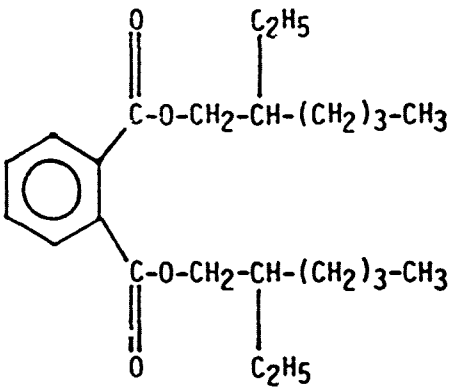
Molecular Structure:



Di-2-ethylhexyl Phthalate. Synonyms: Bis (2-ethylhexyl) Phthalate, DEHP, Di (2-ethylhexyl) orthophthalate, Di-sec-octyl Phthalate, 2-ethylhexyl Phthalate, Flexol DOP, Flexol Plasticizer DOP, Hercoflex DOP.

Molecular Formula: $C_6H_4[COOCH_2CH(C_2H_5)C_4H_9]_2$

Molecular Structure:



Flame Photometer. One of several types of instruments that can be used in flame photometry analysis, such as the emission flame photometer and the atomic absorption spectrophotometer. To analyze an aerosol, a controlled amount of the substance is heated in a flame and the resulting spectral line emission is analyzed for its spectral describing qualities.

Gas. A state of matter in which the molecules move freely, and consequently, the entire mass tends to expand indefinitely, thereby occupying the total volume of any vessel into which it is introduced. Gases will mix freely with each other and they can all be liquified.

Lethal Concentration Fifty. A calculated concentration of a substance in air, exposure to which for a specified length of time is expected to cause the death of 50% of an entire defined experimental animal population as determined from the exposure to the substance of a significant number from that population (LC50).

Lethal Dose Fifty. A calculated dose of a substance which is expected to cause the death of 50% of an entire defined experimental animal population, as determined from the exposure to the substance by any route, other than inhalation, of a significant number from that population (LD50).

Lowest Lethal Concentration. The lowest concentration of a substance in air, other than LC50, which has been reported to have caused death in humans or animals. The reported concentrations may be entered for periods of exposure which are less than 24 hours (acute) and greater than 24 hours (subacute and chronic).

Lowest Lethal Dose. The lowest dose (other than LD50) of a substance introduced by any route, other than inhalation, over any given period of time in one or more divided portions and reported to have caused death in humans or animals.

Lowest Toxic Concentration. The lowest concentration of a substance in air to which humans or animals have been exposed for any given period of time that has been reported to produce any toxic effect in humans or to produce a carcinogenic, teratogenic, mutagenic, or neoplastigenic toxic effect in animals or humans.

Lowest Toxic Dose. The lowest dose of a substance introduced by any route, other than inhalation, over any given period of time and reported to produce any toxic effect in humans or to produce carcinogenic, teratogenic, mutagenic, or neoplastigenic effects in humans or animals.

Light Photometer. An instrument used for making measurements of light describing qualities such as luminous intensity, spectral distribution, absorption, and transmittance and reflectance that are affected when an aerosol is allowed to enter an analyzing chamber.

Nuisance Particulates. In contrast to fibrogenic dusts which cause scar tissue to be formed in lungs when inhaled in excessive account, so-called "nuisance" dusts have a long history of little adverse effect on lungs and do not produce significant organic disease or toxic effect when exposures are kept under reasonable control. The nuisance dusts have also been called (biologically) "inert" dusts, but the latter term is inappropriate to the extent that there is no dust which does not evoke some cellular response in the lung when inhaled in sufficient amount. However, the lung-tissue reaction caused by the inhalation of nuisance dusts has the following characteristics: (1) The architecture of the air spaces remains intact. (2) Collagen (scar tissue) is not formed to a significant extent. (3) The tissue reaction is potentially reversible.

Excessive concentrations of nuisance dusts in the workroom air may seriously reduce visibility, may cause unpleasant deposits in the eyes, ears, and nasal passages (Portland cement dust), or cause injury to the skin or mucous membranes by chemical or mechanical action per se or by the rigorous skin cleansing procedures necessary for their removal.

A threshold limit of 10 mg/m^3, or 30 mppcf, of total dust (<1% quartz), or 5 mg/m^3 respirable dust is recommended for substances in these categories and for which no specific threshold limits have been assigned. This limit for a normal workday does not apply to brief exposures at higher concentrations; neither does it apply to those substances which may cause physiologic impairment at lower concentrations but for which a threshold limit has not yet been adopted.

Simple Asphyxiants. A number of gases and vapors, when present in high concentrations in air, act primarily as a simple asphyxiant without other significant physiologic effects. A TLV may not be recommended for each simple asphyxiant because the limiting factor is the available oxygen. The minimal oxygen content should be 18% by volume under normal atmospheric pressure (equivalent to a partial pressure, pO_2 of 135 millimeters Hg). Atmospheres deficient in O_2 do not provide adequate warning, and most simple asphyxiants are odorless. Several simple asphyxiants present an explosion hazard. Account should be taken of this factor in limiting the concentration of the asphyxiant.

Threshold Limit Value (TLV). The TLV is an American Conference of Governmental Industrial Hygienists recommended upper limit (ceiling) or time-weighted average concentration of a substance to which most workers can be exposed without adverse effect.

Vapor. A substance in the gaseous state, but below its critical temperature, is called a vapor. If a pure liquid partly filling a closed container is allowed to stand, the space above it becomes filled with the vapor of the liquid, which develops a pressure.